ABSTRACTS OF WORLD MEDICINE

VOL. 22 No. 1 JULY, 1957

Pathology

1. **Hemoglobin Concentrations as Determined by a Methemoglobin Method. Studies on 1,000 College Students**

F. K. MORRIS, V. E. LOY, K. M. STRUTZ, L. L. SCHLOESSER, and R. F. SCHILLING. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **26**, 1450–1455, Dec., 1956 [received March, 1957]. 2 figs., 13 refs.

From the University of Wisconsin Medical School, Madison, a method is described for the determination of haemoglobin concentration in which the haemoglobin is converted to cyanmethaemoglobin and estimated by photoelectric colorimeter. In 1,000 young people entering the University, mostly aged between 18 and 25, the haemoglobin values for men ranged from 13·5 to 19·4 (mean 16·4±1·9) g. per 100 ml., and for women from 9·1 to 17·0 (mean 14·3±1·8) g. per 100 ml. These values corresponded closely to reported results obtained by other methods of estimation. *Marjorie Le Vay*

EXPERIMENTAL PATHOLOGY

2. **Serum Glutamic Oxalacetic Transaminase in Experimental Tissue Injury**

L. A. RUDOLPH, J. A. SCHAEFER, R. E. DUTTON, and R. H. LYONS. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **49**, 31–40, Jan., 1957. 7 figs., 7 refs.

At the State University of New York College of Medicine, Syracuse, the serum glutamic oxalacetic transaminase activity was studied in some 70 mongrel dogs which were subjected to experimental infarction or to ischaemia of various organs. At operation every precaution was taken to minimize surgical trauma to the tissues. The experiments were controlled by repeating the operation, with the exception of the application of the arterial ligature or clamp, on a similar dog. In the experiments on the heart a ligature was placed in position at operation and later, under electrocardiographic control, traction was applied to the ligature, the period of ischaemia being determined by elevation of the S-T segment. Other organs were rendered ischaemic by direct clamping of the supplying artery at operation. A rough correlation was observed between the amount of tissue rendered necrotic and the serum enzyme level in experimental myocardial infarction. Elevation of the serum enzyme level was also noted following infarction and necrosis of the kidney, spleen, lungs, and bowel. *P. E. Conen*

3. **The Dynamics of the Extinction and Restoration of Vital Functions after the Lethal Exsanguination of Hypothermic Animals.** (Динамика угасания и восстановления жизненных функций организма при смертельном обескровливании в условиях гипотермии)

V. A. NEGOVSKII and V. I. SOBOLEVA. *Архив Патологии* [*Arkh. Patol.*] **18**, 58–70, No. 6, 1956. 3 figs., 25 refs.

Lethal exsanguination was carried out by the authors in hypothermic dogs. It was found that hypothermia did not delay the process of dying from haemorrhage, for this took much the same time as in control animals. After apparent clinical death the function of the heart was restored, the process of resuscitation requiring periods varying from 30 seconds to 6 minutes. Most of the animals suffered repeated attacks of fibrillation during resuscitation, but these were successfully relieved by a single defibrillatory condensor discharge. Warming of the animals was begun after the restoration of cardiac function and continued until a body temperature of 32° C. was reached; it was noted that too prolonged or too intensive warming proved unfavourable. The use of hypothermia enabled the period during which the animal remained clinically " dead " to be prolonged up to one hour with subsequent complete and permanent resuscitation. *L. Crome*

4. **Morphological Bone Changes in Rats Subjected to Chronic Poisoning with Radioactive Strontium.** (Морфологические изменения костной ткани у крыс при хронической интоксикации радиоактивным стронцием)

N. N. LITVINOV. *Архив Патологии* [*Arkh. Patol.*] **19**, 26–31, No. 1, 1957. 5 figs., 11 refs.

The author has studied the pathological changes in rats to which 0·4 μc. of radioactive strontium was administered intraperitoneally. The ensuing changes were most marked in the metaphyses of the long bones. The rate of cartilaginous ossification diminished during the first month after administration of strontium, while osteoclasis increased. During the following 2 to 4 months there was a gradual return to normal ossification with, however, a premature arrest of bony growth. In the 5th and 6th months immature osseous structures made their appearance and filled the intertrabecular spaces of the metaphysis and the adjoining parts of the diaphysis. This tissue contained atypical osteoblasts, and later osteogenic sarcoma developed at this site in some cases. Still later osteolysis with the formation of new immature bone was seen along the endosteum

of the metaphysis and diaphysis. The histological appearances are described in some detail and illustrated in photomicrographs. *L. Crome*

CHEMICAL PATHOLOGY

5. **Serum-potassium Levels as an Index of Body Content**
C. T. G. FLEAR, W. T. COOKE, and A. QUINTON. *Lancet* [*Lancet*] **1**, 458–459, March 2, 1957. 1 fig., 8 refs.

At the United Birmingham Hospitals the total exchangeable mass of potassium (K_e) has been determined by use of radioactive potassium (^{42}K) and compared with the serum potassium level, which was determined simultaneously. While K_e may not be identical with the total body potassium, it probably represents the mass of potassium most readily available for metabolic interchange.

Analysis of 110 observations made on 80 patients with a wide variety of disorders, of which the most common were steatorrhoea and congestive heart failure, showed that the value for K_e varied from 16 to 123% of the mean normal, but that there was no correlation between K_e and the serum potassium level. The data confirm earlier similar comparisons. A high serum potassium level may be found in the presence of a low exchangeable potassium value and vice versa. The authors point out that these findings show that reliance should not be placed on the serum potassium level in investigating potassium deficiency, but rather on the recognition of the circumstances likely to lead to a loss of potassium, and only secondly on the clinical signs and symptoms and biochemical findings consistent with such loss.
C. L. Cope

6. **Absorption of Iron from the Gastrointestinal Tract. A Comparative Study of the Oral Iron Tolerance Test in Human Beings Using Stable and Radioactive Iron**
E. D. HENLEY, W. N. CHRISTENSON, W. J. GRACE, and H. G. WOLFF. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **4**, 609–618, Nov.–Dec., 1956. 2 figs., 15 refs.

The serum iron level after ingestion of large doses of iron depends not only upon the rate of absorption but also upon the rate of removal of iron from the blood stream. At Cornell University Medical College, New York, an iron tolerance test employing both stable and radioactive iron (^{59}Fe) was performed on 12 healthy control subjects and 21 patients with a variety of diseases. The results of serum iron determinations performed hourly over a 4-hour period, of the later recovery in haemoglobin of ^{59}Fe, and of total iron absorption by stool analysis for content of ^{59}Fe for the two groups are presented in tables. In most instances stable iron was given orally in the form of ferrous ammonium sulphate (1 mg. per kg. body weight) and radioactive iron (10 to 15 μc.) as ferric chloride (0·001 to 0·016 mg. of elemental iron). In a small number of cases ferrous (stable) Fe and ferrous ^{59}Fe (as ferrous gluconate) were given for comparison. All the subjects were fasted from 10 to 16 hours before the test and also during it. Venous blood specimens were drawn immediately before the oral dose of iron and then hourly for 4 hours. The methods of determining the various values are described in detail.

The authors have demonstrated the greatly improved absorption of iron when reduced to the ferrous state, whether by administering ferrous salts or ferric salts along with ascorbic acid, and they confirm the relatively poor absorption of ferric iron. No definite correlation of the type of disease process with the degree of iron absorption could be expected from this small series of cases, but an interesting finding in the 4 patients with coronary occlusion and one with thrombosis of the axillary vein and pulmonary infarction was evidence of generally poor absorption of iron. The relative inaccuracy of serum iron values as an index of iron absorption is emphasized and it is concluded that a technique employing radioactive ferrous iron—thus allowing evaluation of the eventual uptake of iron in haemoglobin and of its total absorption by stool analysis—provides a more useful and reliable measurement of iron absorption than does the iron tolerance test using stable iron salts. *Victor M. Rosenoer*

7. **A New Method of Determining Gastric Acidity in Man without the Introduction of a Stomach Tube.** (Новый метод экстрагастрального (без применения зонда) определения кислотности (свободной соляной кислоты) желудочного сока у человека)
Y. N. USPENSKII. *Советская Медицина* [*Sovetsk Med.*] 41–43, No. 12, Dec., 1956.

For the determination of free hydrochloric acid in the stomach without the use of intubation the author has devised a special apparatus, an acidometer or gastrotonometer, which works on a photo-electric system. It comprises two 6-volt batteries, two photo-elements. a voltmeter, a rheostat, a sensitive galvanometer, and a special miniature *x*-ray tube, the photo-elements being fixed behind the *x*-ray screen or film. Gastric acidity is measured by determining the difference in the density of the gastric shadow recorded galvanometrically immediately before and then 40 to 60 minutes after a test meal; a meal containing 0·2 to 0·3% of caffeine or 5% alcohol without opaque medium is recommended. The galvanometric readings are translated into units of acidity by means of a specially constructed table [not given] which was prepared from a series of preliminary biochemical observations on 18 patients. *R. Crawford*

8. **The Stool Proteolytic Activity in the Diagnosis of Fibrocystic Disease of the Pancreas**
W. M. FYFE. *Scottish Medical Journal* [*Scot. med. J.*] **2**, 66–68, Feb., 1957. 10 refs.

The proteolytic activity of duodenal juice and faeces was studied by the author at the Royal Hospital for Sick Children, Glasgow, in 50 infants under the age of 2 years, the method of Andersen and Early (*Amer. J. Dis. Child.*, 1942, **63**, 891) being used for duodenal juice, and the serial dilution method of Emery (*Arch. Dis. Childh.*, 1952, **27**, 67; *Abstracts of World Medicine*, 1952, **12**, 178) for stools. No proteolytic activity was present in the duodenal juice of 14 infants with a diagnosis of fibrocystic

disease of the pancreas (confirmed at necropsy in 8). There was no detectable proteolytic activity in the stools in 8 of these, and a titre of 1 in 20 or less in the others. Of 2 infants with little proteolytic activity in the duodenal juice, there was no proteolytic activity in the stool of one who at necropsy proved to have fibrocystic disease, and a high stool titre in the other, in whom there was no clinical evidence of fibrocystic disease. The duodenal juice of the remaining 34 children showed normal proteolytic activity, but in 7 the stool titre was 1 in 20 or less.

The author suggests that duodenal intubation is unnecessary where the stool titre is 1 in 40 or more, but should be performed where the titre is 1 in 20 or less in order to assess the activity of the duodenal juice.

M. Lubran

9. **Urinary Osmolar Concentration in the Hydropenic State as a Measure of Renal Tubular Function: a Test for Early Renal Impairment: Preliminary Report**
M. N. FRANK, L. S. DREIFUS, F. RARICK, and S. BELLET. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 121–125, Feb., 1957. 1 fig., 11 refs.

An attempt has been made at the Philadelphia General Hospital to correlate the commonly used tests of renal function, that is, the blood urea nitrogen test, the Fishberg concentration test, and the phenolsulphonphthalein (PSP) test, with the maximum tubular concentration function as measured by urinary osmotic pressure under hydropenic conditions. The values for blood urea nitrogen, urinary specific gravity, and total solute concentration were determined in 32 healthy subjects and in 27 patients with essential hypertension, 13 with diabetes mellitus, and 7 with compensated rheumatic heart disease, while the PSP test was performed only on the patients with hypertension and diabetes mellitus.

In the normal subjects—but not in the patients with essential hypertension, diabetes mellitus, and rheumatic heart disease—a linear correlation was found between the urinary specific gravity and the urinary osmolar concentration; the lack of correlation between these factors in the patients is attributed to the fact that solutes, protein, sugar, temperature, and *p*H value contribute differently to the specific gravity and to the osmotic pressure. It is suggested that the following maximum urinary concentrations (1) over 800 mOsm. per litre, (2) from 800 to 600 mOsm. per litre, (3) from 600 to 400 mOsm. per litre, and (4) less than 400 mOsm. per litre indicate respectively adequate, good, and fair renal function, and severe renal disease. The test for urinary osmotic concentration may be used to evaluate tubular function and to follow the course of renal disease, especially in patients with minimal tubular impairment. The test may often give an earlier indication of renal disease than either of the other urinary function tests or clinical observation.

J. E. Page

10. **An Electrophoretic Study of the Abnormal Proteins in Urine, Peripheral Venous and Bone Marrow Sera in Multiple Myeloma**
R. T. S. JIM. *Blood* [*Blood*] **12**, 56–63, Jan., 1957. 3 figs., 21 refs.

11. **Effect of Renal Disease on the Schilling Test**
C. E. RATH, P. R. MCCURDY, and B. J. DUFFY. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 111–114, Jan. 17, 1957. 2 figs., 9 refs.

A study of the effect of renal disease on the Schilling test—that is, the urinary excretion of cyanocobalamin (vitamin B_{12}) labelled with radioactive cobalt (*J. Lab. clin. Med.*, 1953, **42**, 860; *Abstracts of World Medicine*, 1954, **16**, 42)—is reported from Georgetown University School of Medicine and Hospital, Washington, D.C. The excretion in 29 patients with Addison's pernicious anaemia was less than 6·9% of the orally administered dose of cyanocobalamin, the mean being 1·8%; while 33 control subjects with a variety of disorders (excluding pernicious anaemia and severe renal disease) all excreted more than 8·4% (mean 15·3%). Of 16 patients with severe renal disease, 13 had excretion figures in the pernicious-anaemia range; this was not increased by administration of intrinsic factor in 2 patients. In 7 cases of renal disease, in which collections were continued for several days there was appreciable excretion of the vitamin after the first 24 hours. The authors conclude that renal disease must be considered in the interpretation of excretion in the pernicious-anaemia range, even though the urinary volume is normal and clinical signs of uraemia are absent. They suggest that cases of pernicious anaemia can be distinguished from those of renal disease by the lack of effect of intrinsic factor and the continued excretion of radioactive-cobalt-labelled cyanocobalamin after the first 24 hours in cases of renal disease.

Janet Vaughan

MORBID ANATOMY AND CYTOLOGY

12. **Morphology of Cortical Contusions**
R. LINDENBERG and E. FREYTAG. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] **63**, 23–42, Jan., 1957. 30 figs., 41 refs.

Writing from the Maryland School of Medicine, Baltimore, the authors review the subject of cortical contusions and supplement it with personal experience gained in evaluating some 650 cases of head trauma.

Contusions comprise bruises and lacerations of the cortex caused by mechanical factors, the overlying dura being intact. The primary sequelae are predominantly haemorrhage and tissue necrosis which occur at the moment of impact, though either may be present without the other. Haemorrhages are located at and near the crest of a convolution, and are streak-like, multiple, and densely arranged. They usually increase in size within the first few hours after trauma and, if the individual survives, undergo the usual changes, the final result being a small rust-brown spot if the haemorrhage was small, and glial scarring or cyst formation if it was large.

Areas of contusion necrosis are usually wedge-shaped in cross-section, the base being at the crest of the convolution and the point directed towards or into the white matter. Old lesions appear macroscopically on the surface of the brain as crater-like defects or furrows (and were once thought to be due to arteriosclerosis). The

microscopical appearances in various zones of lesions at various ages are described in detail. The authors conclude that their findings suggest that it is the initial positive-pressure phase of the compression wave caused by the impact which is mainly responsible for the development of contusion necrosis. *R. G. Rushworth*

13. **Changes in the Nerve Cells of the Medulla Oblongata in Hypertension.** (Об изменениях первых клеток продолговатого мозга при гипертонической болезни) A. I. STRUKOV and V. S. MITROFANOV. *Архив Патологии* [*Arkh. Patol.*] **19**, 51–53, No. 1, 1957. 5 figs., 5 refs.

In a series of post-mortem studies it was found that the nerve cells in the medulla oblongata of patients dying from hypertension showed chromatolysis, necrobiosis, unevenness of staining, and shrinkage, these changes being particularly marked in the dorsal nucleus of the vagus nerve. An additional finding was occasional amitotic division of nerve cells, and this is interpreted as a compensatory regenerative phenomenon. The authors discuss these and similar recorded findings in relation to the functional disturbance associated with the excessive load borne by the autonomic nerve centres concerned with innervation of the heart. *L. Crome*

14. **Observations on the Morbid Anatomy of Coronary Artery Disease**
A. W. BRANWOOD and G. L. MONTGOMERY. *Scottish Medical Journal* [*Scot. med. J.*] **1**, 367–375, Dec., 1956. 9 figs., 9 refs.

An investigation of the pathological changes in the heart in 144 cases of sudden death and of clinically diagnosed coronary thrombosis is reported from the University of Edinburgh. The method used was to deep-freeze the heart at −20° C. and to cut it into 2-mm. slices on a meat slicer. This technique was shown to be as efficient and reliable in detecting thrombi as cutting serial sections 100 μ apart from the whole coronary arterial tree, as was carried out on 50 hearts as a check on the first method.

In all of the 26 cases of sudden death outside hospital a previous history of angina was obtained, and in none was an extracardiac cause of death found. Only 8 of these cases, however, showed coronary occlusion by recent thrombus or atheromatous softening; in 6 there was a non-occlusive thrombus and the rest showed no occluding material. There were 6 cases of recent infarction, only 3 of which had thrombi. In all cases there was gross atheromatous stenosis of all the coronary arteries and also evidence of myocardial fibrosis. In all 13 cases of sudden death in hospital (mainly post-operative) there was severe coronary stenosis and myocardial fibrosis; in this group were 3 recent infarcts without thrombosis and 3 cases of recent thrombosis.

Of the largest group examined, namely, 101 cases of clinical coronary thrombosis confirmed by electrocardiography, a recent infarct was found at necropsy in only 61, myocardial fibrosis alone in 25, minor muscle changes of dubious significance in 10, and no evidence of infarct or fibrosis in 5. Of the 61 cases of infarction, coronary occlusion was found in 24; in the rest non-occlusive thrombus was present in 23, no recent thrombus was detected in 13, and coronary embolism in one case, in a woman aged 58 who had undergone an operation on the gall-bladder on the previous day. In the great majority of cases severe stenosis affected all three coronary arteries. Further, since only about 40% of cases of infarction had a coronary occlusion the authors conclude that infarction is related to over-all coronary insufficiency rather than to occlusion of a particular artery.

Assessment of the age of the thrombi and infarcts by histological criteria showed that while most infarcts were at least several days old, the associated coronary thrombi appeared to be only 24 to 36 hours old. Therefore, the authors conclude, unless the sequence of histological changes in thrombi is very much delayed in atheromatous coronary arteries, it would seem that coronary thrombosis is often not the cause, but the terminal event in the presence of an already established recent myocardial infarct.

[An incidental finding of much interest was that in some cases the fatty material in the atheromatous plaques had excited an intense local foreign-body reaction. This unusual response would be worth investigating, since such plaques are particularly liable to rupture.]
M. C. Berenbaum

15. **The Manner of Death in Coronary Artery Disease**
J. H. MOWBRAY and J. D. HAMILTON. *Canadian Medical Association Journal* [*Canad. méd. Ass. J.*] **76**, 9–15, Jan. 1, 1957. 9 refs.

The authors first describe, from the University of Toronto, a method of treating the coronary arteries which permits of a thorough examination, both gross and microscopical, of lesions of these vessels. At necropsy the heart was removed intact with part of the aorta, and the coronary vessels were perfused through the aorta with saline at roughly mid-diastolic pressure to remove fluid blood, and then similarly for one hour with 10% formalin in order to fix them *in situ*; when fixed, they were dissected clear of the heart down to the smaller surface branches (about 1 mm. in diameter), decalcified, and cleared by successive immersions, the whole process resulting in " a set of semitranslucent, moderately pliable tubes ". As a result the more opaque arteriosclerotic plaques and the reddish-black lesions containing clotted blood could be seen from the outside, and the significant lesions, thus clearly visible on gross examination, could be selected for multiple microscopical sectioning.

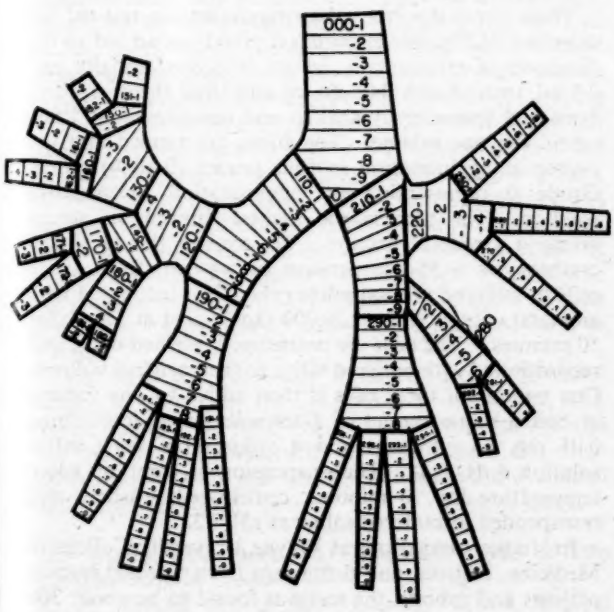
Employing this method the authors have studied the coronary arteries in 100 cases coming to necropsy, in 22 of which death was due to disease related in one way or another to the coronary arteries. After discussing the existing considerable confusion in medical literature concerning the use of such terms as " acute coronary failure ", " acute coronary insufficiency ", and others, they analyse their cases from the anatomical as well as from the clinical standpoint. In about half of the patients with abrupt onset of ischaemic cardiac pain coronary thrombosis and corresponding recent myocardial infarcts were found. The other half included

cases of focal myocardial necrosis (with no trace of recent thrombosis), acute thrombosis with no infarct (the latter being precluded by the patient's early death), cases of " sudden death " with no anatomical lesion other than coronary stenosis or myocardial scarring, and one case of coronary embolism. The clinical data supported the histological findings, thus suggesting that there is frequent recurrent thrombosis. This study once more underlines the importance of counteracting by anticoagulant therapy the thrombotic tendency apparently existing in patients with myocardial infarcts.

[Although the 22 cases of coronary arterial disease represents rather a small series the method described for the preparation of the coronary arteries deserves the attention of all concerned with the morbid anatomy of cardiac failure. A large-scale study on these lines might yield valuable new information.] *F. S. Freisinger*

16. **Changes in the Bronchial Epithelium in Relation to Smoking and Cancer of the Lung. A Report of Progress**
O. Auerbach, J. B. Gere, J. B. Forman, T. G. Petrick, H. J. Smolin, G. E. Muehsam, D. Y. Kassouny, and A. P. Stout. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 97–104, Jan. 17, 1957. 11 figs., 39 refs.

To investigate the histological changes in the bronchial epithelium in relation to smoking and the occurrence of lung cancer a painstaking microscopical study of the bronchial tree was carried out on 117 patients who came to necropsy at the Veterans Administration Hospital, East Orange, New Jersey, and whose smoking habits



Schematic diagram of tracheo-bronchial tree, showing distribution of 208 sections.

were known. The trachea and main bronchi were dissected out, subdivided into 208 blocks (see diagram), and from each block one section was cut and stained. Amongst the 117 patients were 34 who had died of bronchogenic carcinoma, and all of these were smokers. The remaining 83 (non-cancer) patients were subdivided into non-smokers, moderate smokers, and heavy smokers. The epithelial changes observed were designated " basal-cell hyperplasia " (consisting of at least 3 rows of cells), " stratification ", " squamous metaplasia ", and " carcinoma *in situ* ", and all of these were found in all groups. However, with increasing cigarette consumption there was a progressive rise in their incidence, which was constantly highest in the cancer group. Attention is drawn to the fact that the percentage of carcinoma *in situ* was practically as high in the heavy smokers of the non-cancer group as in the cancer group (6·0 and 6·3 respectively), and this change was found in many widely distributed areas of the bronchial tree. The authors interpret their findings as being consistent with the hypothesis that inhaled substances are important factors in the causation of bronchogenic carcinoma, and also with the hypothesis that cigarette smoke is one of these.
R. Salm

17. **Anterior Pituitary Glands in Patients Treated with Cortisone and Corticotropin**
R. A. Kilby, W. A. Bennett, and R. G. Sprague. *American Journal of Pathology* [*Amer. J. Path.*] **33**, 155–173, Jan.–Feb., 1957. 9 figs., 48 refs.

18. **The Demonstration of Malignant Cells Exfoliated from the Proximal Colon**
W. C. Ebeling and J. W. Little. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 21–29, Jan., 1957. 6 figs., 4 refs.

From University Hospital, Baltimore, Maryland, is described a method for cytological diagnosis of carcinoma of the colon which is particularly useful for cases in which the neoplasm is beyond the range of the sigmoidoscope and where radiological reports are negative, doubtful, or conflict with the clinical diagnosis. After administration of tap-water enemata, repeated until the return is clear, the patient is placed in the left lateral position and a rubber catheter inserted rectally to 20 cm., through which 250 ml. of unheated 0·9% saline solution is then poured into the bowel. The catheter is clamped and, the patient having been rolled on to his back, the abdominal wall over the large intestine is massaged with deep pressure. After lying for a while in the right lateral position the patient is moved back into the left lateral position and the saline solution recovered by siphonage into a specimen bottle. The specimen is centrifuged at 1,000 r.p.m. for 35 minutes and the sediment smeared on to four slides and fixed in 95% ethyl alcohol and ethyl ether for 12 hours. Staining follows. Malignant cells are distinguished from normal cells by their size, the dark, large, irregular nuclei, and the scanty cytoplasm.

Eight illustrative cases are recorded where cytological diagnosis preceded the correct radiological or operative diagnosis, in none of which was the lesion accessible to the sigmoidoscope, 4 of the carcinomata in these cases being caecal. *J. Naish*

Microbiology and Parasitology

19. **Comparative Efficacy of Direct Microscopy (Two Methods) and Cultures in the Diagnosis of Tuberculosis**
G. M. NEEDHAM. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **32**, 1–5, Jan. 9, 1957. 5 refs.

The purpose of this report is to summarize experience at the Mayo Clinic with the Ziehl–Neelsen technique and the auramine-O fluorescent procedure as methods for demonstrating tubercle bacilli in pathological material. Findings were checked by culture on Löwenstein–Jensen medium. Specimens included sputum, bronchial secretions, urine both voided and obtained by catheter, pleural fluid, cerebrospinal fluid, and material removed at operation and necropsy, but not gastric contents. Of 22,445 specimens examined, 19,213 were negative both on microscopical examination and on culture. Positive cultures were obtained with 3,073 specimens, and it is of particular interest to observe that 1,699 (55%) of these gave negative results on direct microscopy. The fluorescent technique yielded a slightly greater proportion of positive smears than did the Ziehl–Neelsen method. Morphologically typical tubercle bacilli which proved to be non-viable were found in 159 cases. It is concluded that in the diagnosis of tuberculosis the demonstration of acid-fast bacilli by culture and inoculation of animals is superior to the direct microscopical procedures evaluated in this study. *E. G. Rees*

20. **Flocculation Tests for Brucellosis**
C. A. HUNTER and B. COLBERT. *Journal of Immunology* [*J. Immunol.*] **77**, 232–241, Oct., 1956. 3 figs., 33 refs.

In this paper from the Topeka (Kansas) Public Health Laboratory are reported a continuation of the authors' experiments on flocculation tests for brucellosis in which *Brucella* extract adsorbed on cholesterol crystals in the presence of lecithin is used as an antigen. An emulsion of this antigen is also used in a microscopical slide test and a macroscopical tube test. Full details are given of both these tests and of the preparation of all the reagents and of the *Brucella* extract, and a method of standardizing the antigen is described. Serum absorption experiments showed that the antigen emulsion was specific for *Brucella*. The two flocculation tests were compared with an agglutination test by carrying out all three tests in parallel on 100 specimens of human and 100 of bovine serum.

Flocculation tests gave better results, and agglutination tests have now been discontinued at this laboratory, which tests 100,000 sera for *Brucella* each year. Pre-zone reactions were not found with the flocculation tests when human sera were being tested, but were present in some bovine sera. Heating the serum to 56° C. for 30 minutes prevented this pre-zone reaction and also the reaction which occurred with human sera tested by agglutination methods. *P. E. Conen*

21. **Immunization of Infants with Living Attenuated Poliomyelitis Virus. Laboratory Investigations of Alimentary Infection and Antibody Response in Infants under Six Months of Age with Congenitally Acquired Antibodies**
H. KOPROWSKI, T. W. NORTON, K. HUMMELER, J. STOKES, A. D. HUNT, A. FLACK, and G. A. JERVIS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **162**, 1281–1288, Dec. 1, 1956. 3 figs., 18 refs.

Living attenuated poliomyelitis virus was administered by the oral route to 24 infants. Sixteen received SM (Type 1) virus alone, 2 the TN (Type 2), and 6 both viruses at different times. All the infants were under 6 months old; the ages of 6 were between 10 and 27 days. Most of them had antibodies acquired from their mothers to the virus fed. All infants developed active immunity after inapparent alimentary infection. High levels of homotypic antibodies caused by the feeding of virus were maintained during an observation period of 7 months.—[Authors' summary.]

22. **Use of Hemagglutination in the Diagnosis of Trichinosis**
S. G. PRICE and L. M. WEINER. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **26**, 1261–1269, Nov., 1956 [received Jan., 1957]. 11 refs.

The authors describe a haemagglutination test for the detection of *Trichinella spiralis* antibody as an aid to the diagnosis of trichinosis. Serum is diluted serially and 0·5 ml. treated with 0·05 ml. of sensitized sheep erythrocytes and immediately shaken and centrifuged at 1,800 r.p.m. for one minute. The tubes are tapped and the degree of agglutination in four grades (0 to 4) noted, Grade 0 representing no agglutination or negative reaction. The titre is the highest dilution of serum giving a Grade-2 reaction. To prepare the sensitized erythrocytes a 5% suspension of washed, fresh sheep cells in buffered normal saline (*p*H 7·2) is incubated with an equal volume of 1 in 20,000 tannic acid at 37° C. for 10 minutes. The cells are centrifuged, washed once, and reconstituted with buffered saline to their original volume. One volume of these cells is then added to one volume of boiled saline extract of *Trichinella* larvae (containing 0·05 mg. of nitrogen) and 4 volumes of 0·9% saline solution (*p*H 6·4). The suspension is kept at room temperature for 10 minutes, centrifuged, washed, and resuspended in buffered saline at *p*H 7·2.

In studies carried out at Wayne University College of Medicine, Detroit, and using sera from infected human patients and rabbits, the test was found to be about 300 times more sensitive than the precipitin test and 100 times more sensitive than the complement-fixation test. A preliminary evaluation of the test has shown no false positive reactions with 25 normal sera and 25 other sera from patients with positive Kahn reactions, dermatomyositis, rheumatic fever, or brucellosis. *M. Lubran*

Pharmacology

23. **Clinical and Laboratory Assessments of Senna Preparations**
J. C. McC. Browne, V. Edmunds, J. W. Fairbairn, and D. D. Reid. *British Medical Journal* [*Brit. med. J.*] 1, 436–439, Feb. 23, 1957. 7 refs.

In this trial, carried out at two London hospitals, the laxative effects of two *B.P.* senna syrups were compared with those of a dried preparation of senna pods ("senokot") and of an inert control substance. Both short-term (obstetric) and long-term (chronic elderly) patients took part in the trial. The aqueous *B.P.* preparations proved unreliable, and chemical assay confirmed deterioration in them; they were often without any effect at all. The dried preparation was a consistently potent laxative.
P. Mestitz

24. **The Clinical Value of Toclase in Suppressing the Cough Reflex**
C. H. Carter and M. C. Maley. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 77–79, Jan., 1957. 3 refs.

A clinical trial of a new antitussive agent, carbetapentane ("toclase"), which has been claimed to be superior to codeine in suppressing the cough reflex in experimental animals, is here reported. Toclase was administered to 557 patients with cough accompanying a variety of respiratory disorders. Single doses of 7 to 25 mg. in tablet or liquid form were given in a total dosage up to 150 mg. daily for 5 days or until the patient was free of cough. The drug proved effective in relieving the cough in 505 (90·7%) of the 557 patients treated, irrespective of the causal disease. The liquid form of the medication proved to be slightly superior to the tablets. Side-effects were negligible. Of a control group of 134 patients treated with inert tablets similar in appearance to those containing toclase, only 7 (5·2%) reported benefit. The recommended dose of toclase is 7 to 10 mg. for children and 25 mg. for adults. The effect of such doses was apparent in 15 minutes and persisted for 4 to 6 hours.

[The value of this study is limited by the authors' failure to adhere to the recognized principles of such trials, notably the need for a double-blind design and the ensuring of homogeneity as regards age, sex, diagnosis, and duration and severity of disease in the control and treated groups.] *Bernard Isaacs*

25. **Aspirin Intolerance. A Comparative Trial of Two Modified Aspirin Products**
R. M. Vining and G. D. Kersley. *British Medical Journal* [*Brit. med. J.*] 1, 444–445, Feb. 23, 1957. 6 refs.

Two modified aspirin preparations—"paynocil", an aspirin and glycine combination, and "disprin", a citrated preparation—were investigated at the Royal National Hospital for Rheumatic Diseases, Bath. Of 178 patients with rheumatic diseases, 45 (25%) proved intolerant of ordinary aspirin; of these, 37 (82%) were able to take one of the other two tablets, preferences being equally divided amongst the two. No significant differences in analgesic effect were found between paynocil and disprin. *P. Mestitz*

26. **Chlorpromazine as an Adjuvant in the Relief of Chronic Pain**
J. W. Dundee. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **29**, 28–34, Jan., 1957. 37 refs.

Chlorpromazine by mouth potentiates the analgesic action of morphine, pethidine, acetylsalicylic acid, and phenacetin. It is reported to have "a central action, which has been termed 'pharmacological frontal leucotomy'"; it is a powerful anti-emetic. This paper from the University of Liverpool reports the use of this drug on 76 patients, one-third of whom were suffering from pain caused by malignant disease. The initial daily dose was 25 mg., this being increased if necessary to 250 mg. daily. No difficulty in withdrawal was encountered in patients subjected to surgery. The duration of treatment varied from one week to more than 6 months.

It was found that chlorpromazine alone possessed little analgesic power, but it appeared to assist the action of other analgesics, especially levorphanol ("dromoran") and papaveretum. Drowsiness, pyrexia, dryness of the mouth, and loss of appetite were the commonest side-effects encountered, occurring in some two-thirds of the cases, but withdrawal of the drug was necessary in only 2 cases. Jaundice developed in one case. The author states that the dangers associated with chlorpromazine do not appear to be sufficiently great to preclude its use in patients suffering pain from malignant disease.
W. Stanley Sykes

27. **Trials with Carbocaine. A New Local Anaesthetic Drug**
B. af Ekenstam, B. Egnér, L. R. Ulfendahl, K. G. Dhunér, and O. Oljelund. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **28**, 503–506, Nov., 1956.

The use as analgesics of a new series of synthetic preparations—hydrated pyridine carboxylic acids—has been studied at a number of centres in Sweden, the clinical trials having been conducted at the Sahlgren Hospital (University of Gothenburg). The preparation most extensively studied—DL-N-methyl-pipecolic acid 2:6-dimethylanilide—has been given the name of "carbocaine". Experiments on dogs and rabbits showed that it is about as potent as lignocaine, but less toxic and longer-lasting. It was used clinically in 652 cases for blocks of various types and was found to give satisfactory results. In caudal analgesia it was confirmed that its effect outlasted that of lignocaine.
Ronald Woolmer

Chemotherapy

28. **The Prolonged Administration of Streptomycin Hydrosulfate. The Effect on Hearing**
I. S. WITCHELL. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **64**, 514–519, Dec., 1956. 9 refs.

An audiological study was made at Montefiore Hospital, New York, of 102 patients who had been taking streptomycin for 18 months or more, 20 being in-patients, and 82 out-patients. The usual course of treatment was 1 g. daily for 7 to 30 days, then 1 g. thrice or twice weekly. The average period of treatment was 38 months and the average total dose 377 g. Of the 102 patients, 39 showed hearing loss after an average period of treatment of 36 months and an average total dose of 345 g. Only 8 patients in the whole group complained of defective hearing; in the others the loss was detected by the audiometric examination. It is noted that the hearing loss was detected much more frequently among older patients, the incidence being 21% in the age group 13–29 years and 62% in the age group 50–59 years. *F. W. Watkyn-Thomas*

29. **Antibiotic Combinations. Antistreptococcal and Antistaphylococcal Activity of Plasma of Normal Subjects after Oral Doses of Penicillin, Oleandomycin and Combinations of These Antibiotics**
W. F. JONES and M. FINLAND. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 115–119, Jan. 17, 1957. 5 figs., 8 refs.

Controlled studies of the antistreptococcal and antistaphylococcal activity of plasma were carried out in subjects receiving penicillin alone, oleandomycin alone and various combinations of these two agents. Penicillin produced the highest peak values and the greatest total amount of activity in the blood against penicillin-sensitive strains. Oleandomycin was the least active, although with a large single dose, the activity was slightly more prolonged than that of a similar amount of penicillin in some of the subjects. The combinations of penicillin with oleandomycin always gave intermediate values. No enhanced activity of any of the combinations of oleandomycin and penicillin was demonstrable. —[Authors' summary.]

30. **Clinical Experience with "Romicil" (Oleandomycin), a New Antibiotic.** (Klinische Erfahrungen mit Romicil (Oleandomycin), einem neuen Antibiotikum)
W. SIEGENTHALER, G. KEISER, and R. HEGGLIN. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **81**, 2074–2082, Dec. 21, 1956. 7 figs., 11 refs.

In this paper from the Cantonal Hospital, St. Gallen, Switzerland, are described the authors' experience in the treatment of 216 cases of various infections with "romicil" (oleandomycin), of which adults were given daily doses of 1·5 to 2·0 g. every 6 hours, and children received 40 mg. per kg. body weight daily. No side-effects were noted even with much higher doses, up to 5 g. per day.

In the whole series treated there was only one instance of enterocolitis, and this could not be related with certainty to the drug. Primary and secondary resistance to oleandomycin was encountered in some cases; in general the antibiotic spectrum was similar to that of erythromycin.

Apart from the bacterial conditions, in which a broad-spectrum antibiotic would be expected to give good results, there were some indications that oleandomycin affected favourably cases of atypical pneumonia, Q fever, and leptospirosis, while 6 patients who were carriers of *Corynebacterium diphtheriae* were cleared of their carrier state.

The authors conclude that on the grounds of its wide range of activity and also of its notable lack of side-effects oleandomycin is a worth-while antibiotic in hospital and family practice. Because of the development of bacterial resistance, however, they consider that it will probably be best administered in combination with some other drug if a synergist to it can be found. *I. A. B. Cathie*

31. **Studies in the Chemotherapy of Tuberculosis: Ethyl Mercaptan and Related Compounds**
G. E. DAVIES, G. W. DRIVER, E. HOGGARTH, A. R. MARTIN, M. F. C. PAIGE, F. L. ROSE, and B. R. WILSON. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **11**, 351–356, Dec., 1956. 4 refs.

An investigation of the antituberculous activity of the sodium thiosulphates showed that sodium S-ethylthiosulphate was the only active compound, and that diethylsulphide, to which S-ethylthiosulphate decomposed on storage, had marked antituberculous activity. Both these compounds can be decomposed to ethyl mercaptan, which is also antituberculous in mice. The authors consider it probable that some metabolite of ethyl mercaptan is the actual active agent. Ethyl mercaptan is therapeutically unacceptable because of its odour, but further investigation showed that the group of ethyl thioesters released the thiol after absorption, and that one member of this group, ethyl thiobenzoate, had marked antituberculous action. Work on this group of drugs is continuing, and there is a possibility that they may prove useful in the treatment of tuberculosis in human beings. *Paul B. Woolley*

32. **Relationship of Isoniazid to the Metabolism of Mycobacteria. Catalase and Peroxidase**
M. O. TIRUNARAYANAN and W. A. VISCHER. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **75**, 62–70, Jan., 1957. 14 refs.

Infectious Diseases

33. **The Diagnosis of Boeck's Sarcoid by Skeletal Muscle Biopsy. Report of Four Cases**
R. W. PHILLIPS and A. M. PHILLIPS. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **98**, 732–736, Dec., 1956. 4 figs., 9 refs.

Random skeletal muscle (gastrocnemius) biopsy was performed in 5 cases of suspected sarcoidosis at the Veterans Administration Hospital, Providence, Rhode Island. In 4 of the cases the biopsy material showed miliary granulomata consistent with sarcoid tissue; confirmatory histological evidence of sarcoid tissue was obtained from a lymph node in 2 of these and from the skin in another. In none of the cases was there clinical evidence of muscle involvement.

[Before accepting this method of blind biopsy for histological confirmation of sarcoidosis, it is important to know whether similar miliary granulomata are to be found in other granulomatous infections. The authors provide no data on this essential control.]

D. Geraint James

VIRUS DISEASES

34. **Isolation of Echo Virus Type 6 during Outbreak of Seasonal Aseptic Meningitis**
D. T. KARZON, A. L. BARRON, W. WINKELSTEIN, and S. COHEN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **162**, 1298–1303, Dec. 1, 1956. 17 refs.

An outbreak of aseptic meningitis, involving 24 cases, including 7 hospitalized children, occurred in Holland, N.Y., population 500, in July, 1955. The predominant clinical symptoms and signs included fever, frontal headache, signs of meningeal irritation, nausea and vomiting, generalized vague pains, minimal transitory muscle weakness, depression of superficial and deep tendon reflexes, and pharyngeal injection. All patients had a pleocytosis, predominantly lymphocytic. ECHO [enteric cytopathogenic human orphans] virus type 6 was isolated from 7 stools and 4 pharyngeal specimens of 7 hospitalized children, from 2 of 10 stools and none of 6 pharyngeal specimens of 13 healthy household associates, and from one of 3 stools of 3 nonhospitalized patients. All 7 hospitalized patients developed a neutralizing antibody response to ECHO virus type 6 beginning on the fifth day of illness. The antibody was still present after 7 months. Pooled human gamma globulin had a neutralizing antibody titer of 32 against this agent. In addition, 10 orphan agents were isolated from the spinal fluids of patients in other communities during the course of a subsequent generalized outbreak of seasonal aseptic meningitis in western New York. Seven of these agents were identified as ECHO virus type 6. The high virus recovery rate from stool and pharynx, the epidemiological data, the neutralizing antibody response during the course of illness, and the demonstration of virus in the spinal fluid of patients are presented as evidence for establishing an etiological role for ECHO virus type 6 in seasonal aseptic meningitis.—[Authors' summary.]

35. **An Outbreak of Aseptic Meningitis of Virus Origin in East Suffolk**
D. G. GARNETT, A. BURLINGHAM, and D. VAN ZWANENBERG. *Lancet* [*Lancet*] **1**, 500–502, March 9, 1957. 3 refs.

During September and October, 1955, upwards of 130 cases of a new illness suggestive of meningeal irritation appeared in a rural district and a small town in East Anglia.

The first and also the worst cases occurred in young adults, but nearly half the patients were aged 5 to 11 and the oldest was 51. The incubation period was 2 to 4 days. Fever, frontal headache, nausea and vomiting, stiff neck, flushed face, and white tongue were usual. More than 25% of the patients had a macular rash, blotchy on the face and rubelliform elsewhere. The illness lasted a few days only and recovery was complete, but relapse occurred in 7 cases. Fifteen patients were admitted to hospital. The cerebrospinal fluid from 11 of these cases gave cell counts of 200 to 1,000 per c.mm., with a predominance at first of polymorphonuclear leucocytes and later of lymphocytes, and protein levels up to 60 mg. per 100 ml. Strains of virus related to ECHO virus Type 9 were isolated from faeces, from throat washings, or from cerebrospinal fluid of 8 of these patients [see Abstract 36]. *G. C. R. Morris*

36. **Isolation of Viruses Related to ECHO Virus Type 9 from Outbreaks of Aseptic Meningitis**
G. P. B. BOISSARD, L. J. STOKES, A. D. MACRAE, and F. O. MACCALLUM. *Lancet* [*Lancet*] **1**, 500, March 9, 1957. 3 refs.

Results of examination of cerebrospinal fluid, throat washings, and faeces from 11 of the patients in an outbreak of aseptic meningitis in East Suffolk [see Abstract 35] are reported from the Virus Research Laboratory, Colindale, London. These materials were inoculated into tissue-culture tubes of HeLa cells and of monkey-tissue first-passage cells. Cytopathogenic agents were readily isolated from monkey-tissue but not HeLa cells, positive results being obtained from 6 out of 11 specimens of faeces, 4 out of 10 throat washings, and 5 out of 9 specimens of cerebrospinal fluid. Virus strains thus isolated were not neutralized by antiserum against poliomyelitis virus or against Coxsackie viruses Group A Type 9 or Group B Types 1–5. Inoculation into newborn mice of tissue-fluid suspensions of the newly isolated strains caused varying degrees of muscle necrosis in some of the animals, the lesions suggesting an infection with the Coxsackie-A group of viruses. Tests with other

possible aetiological agents were negative. Convalescent sera neutralized the new strains, as did an antiserum against one of them prepared in a rhesus monkey. This antiserum has been found to neutralize virus strains isolated from other outbreaks of aseptic meningitis, and also the prototype Hill strain of ECHO virus Type 9. *G. C. R. Morris*

37. **Meningitis of Virus Origin**

C. E. ROTEM. *Lancet* [*Lancet*] **1**, 502–504, March 9, 1957. 11 refs.

During the summer and autumn of 1956 an outbreak of a disease designated "meningitis of virus origin" occurred in Leicester, and in this paper are reported the first 100 cases admitted to the local isolation hospital. Nearly half the patients were under 11 years of age. The illness resembled non-paralytic poliomyelitis, but was shorter and less severe. A history of contact was common, especially within families. The onset was often sudden. Fever, headache, stiffness of neck and back, and vomiting were usual, and 18 patients had a maculopapular rash. The leucocyte count was normal or almost normal. The cerebrospinal fluid (C.S.F.) was abnormal on admission in 73 cases, and later in 6 more. The C.S.F. cell count was usually below 500 per c.mm., lymphocytes predominating; protein values of 36 to 150 mg. per 100 ml. were found in 41 cases, otherwise protein levels were normal. Two illustrative case histories are given.

At the Virus Reference Laboratory, Colindale, London, a virus similar to ECHO virus Type 9 [see Abstract 36] was isolated from material from 22 patients. In neutralization tests a positive result was obtained with the sera of 22 patients, using the virus isolated from one of them.

The importance of lumbar puncture in differential diagnosis is stressed. No other treatment beyond rest in bed and the administration of analgesics was necessary. Recovery was always complete, though headache and tiredness sometimes persisted for weeks. The relation of the disease to other similar outbreaks recently reported is discussed. *G. C. R. Morris*

38. **Encephalitis and Thrombocytopenic Purpura after Rubella**

E. STEEN and K. H. TORP. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 470–473, Dec., 1956. 1 fig., 32 refs.

The authors discuss the literature concerning serious complications of rubella and describe 3 cases of encephalitis (in 2 boys aged 9 years and a girl of 10 years) and 2 cases of thrombocytopenic purpura (in girls aged 4 and 7 years) complicating rubella. All the patients were admitted to the Ullevål Hospital, Oslo, during the summer of 1955.

The encephalitic cases were characterized by headache and drowsiness, and one patient had right-sided convulsions for 24 hours. Symptoms occurred in one case 2 days before, and in the others 4 and 5 days respectively after, the rash [not described] appeared. They subsided rapidly in all cases and recovery was complete. The cerebrospinal fluid (C.S.F.) was examined in all cases and showed a moderate pleocytosis, lymphocytes predominating, with normal sugar and protein levels except in the case of the boy with convulsions, whose C.S.F. contained 106 mg. of sugar per 100 ml. and whose blood sugar level was 222 mg. per 100 ml. In this case electroencephalography was carried out on the day after admission, when the dominating feature was a generalized rhythmic delta–theta activity of high amplitude at 2 to 3 waves per second, especially on the left side. These changes were subsiding after 10 days, and 38 days later the tracing was normal.

Of the thrombocytopenic cases, haemorrhages and purpura occurred with the onset of the rash in one and 3 days later in the other. The platelet counts varied from 16,200 per c.mm. to 54,000 per c.mm., the bleeding time was more than 15 minutes, and the other haematological findings were normal. The more severe case (in a girl of 7 years) was treated with blood transfusions [amount not stated] and cortisone, 1·25 g. in 12 days. A slight thrombocytopenia [of which the details are not given] was present in one case 4 weeks and in the other 6 months later.

[The clinical and pathological details given are incomplete and there is no mention of differential diagnosis. Nervous and haemorrhagic symptoms occur in glandular fever, and a morbilliform or rubelliform rash may occur in this disease and in ECHO virus infection, neither of which was present.] *I. M. Librach*

39. **Infection with Sendai Virus in an Outbreak of Respiratory Illness**

G. B. B. WHITE, P. S. GARDNER, and R. E. H. SIMPSON. *British Medical Journal* [*Brit. med. J.*] **1**, 381–383, Feb. 16, 1957. 6 refs.

The authors describe investigations carried out at the Virus Reference Laboratory, Colindale, London, and the Public Health Laboratory, Cirencester, in connexion with an outbreak of respiratory infection which occurred in a hospital for the chronic sick and involved 67 out of a total of 180 patients, of whom 21 died. Initially the illness was thought to be due to influenza-A virus which was prevalent in the district at the time, but only 13 out of 38 patients showed a rise of titre in the complement-fixation (C.F.) and the haemagglutination inhibition (H.A.I.) tests. In view of the small number of positive results the sera were retested by the same methods, but using Sendai virus (W.I.C. 12827) and mumps virus (Enders E 63/2) as antigen. A brief outline of the techniques employed is given.

Of the elderly patients who were serologically negative for influenza-A and mumps virus, 5 showed a rising antibody titre in C.F. and H.A.I. tests against Sendai virus. An [unspecified] further number of patients in the hospital and in the town of Cirencester also showed evidence of recent infection with Sendai virus. A third specimen of serum, taken 3 months later, confirmed this impression. Further, a laboratory technician who had collected the blood from one of the patients showed a rising titre against Sendai virus after a mild illness, and 8 out of 49 blood donors in the town who were tested

at the time of the outbreak showed positive C.F. titres against Sendai virus of 1:8 or higher.

In view of some similarity between Sendai virus and the virus of Newcastle disease, and also between the latter and mumps virus, all sera were tested also against complement-fixing mumps-virus particles. With one exception none of the 6 patients with rising Sendai C.F. titres and none of the 5 with unchanging Sendai C.F. titre showed any antibody against mumps virus at a serum dilution of 1:8. None of the sera negative for Sendai at 1:8 had any antibody against mumps virus. Preliminary surveys suggest that antibody to Sendai virus is not uncommon in southern England.

F. Hillman

40. **Latent Infections with Viruses and Rickettsiae**
M. G. P. STOKER. *British Medical Journal* [*Brit. med. J.*] **1**, 963–968, April 27, 1957. 3 figs., 31 refs.

BACTERIAL DISEASES

41. **The Results of Treatment of Diphtheria with Penicillin Alone.** (Les résultats du traitement de la diphtérie par la pénicilline seule)
A. AKKOYUNLU. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **13**, 1065–1068, 1956. 9 refs.

After 12 cases of bacteriologically positive but clinically abortive diphtheria had been successfully treated with penicillin alone all cases clinically diagnosed as diphtheria admitted to the Children's Hospital, Istanbul, which had not been previously treated with antiserum were given 500,000 units of penicillin every 6 to 8 hours and carefully examined daily, both clinically and bacteriologically, until 3 days after a negative culture had been obtained. Supporting treatment consisted in the administration of cardiac stimulants where necessary, of vitamins B and C, adrenocortical hormones, and of strychnine or "sympathol" in cases with circulatory insufficiency.

Of 23 patients with croup thus treated, 13 recovered without tracheotomy in an average time of 4·8 days and a mean period in hospital of 6·5 days. In the 10 cases in which tracheotomy was required the tube was removed within 3·5 days, cultures became negative in 1 to 2 days, and the patients were discharged after 10·5 days. Treatment with penicillin alone did not aggravate the clinical condition and none of the patients developed paralysis.

Of 25 patients with bacteriologically confirmed faucial diphtheria, 22 recovered without any complications. One patient with malignant diphtheria, one with myocarditis, and one who developed faucial diphtheria as a complication of measles and bronchopneumonia died; in these cases it is thought that antiserum would not have altered the outcome except perhaps in the case of malignant diphtheria. In general, cultures became negative in an average of 1·7 days, the false membranes disappeared in 3·2 days, clinical cure was achieved in 4·4 days, and discharge took place after 8 days. The case fatality rate was 8·1%, compared with 11·6% in a series of 43 cases in another clinic in Istanbul where treatment was with a combination of antiserum and penicillin.

These favourable results obtained with penicillin alone lead the author to speculate on the possibility of there being an antitoxic quality present in penicillin, as was first suggested by Ramon *et al.* (*Presse méd.*, 1946, **54**, 637) on the basis of experiments *in vitro* with crude penicillin filtrates. It is regarded as important that one of the advantages of penicillin (as compared with antiserum) is that injections can be repeated without incurring the risk of anaphylactic shock and that it is therefore to be preferred in all cases which have previously received serum therapy.

K. Zinnemann

42. **Brucellosis in Children**
H. R. E. WALLIS. *British Medical Journal* [*Brit. med. J.*] **1**, 617–621, March 16, 1957. 26 refs.

Brucellosis is a common disease in country districts but is often unrecognized. Country children and city children recently returned from holidays in the country in whom there are symptoms of an obscure, prolonged, or relapsing febrile illness may be suffering from infection with *Brucella abortus*. In this paper from Bath Clinical Area, 10 cases of brucellosis are described. The chief clinical features were fever, enlargement of the liver, spleen, or lymph nodes, arthritis, epistaxis, and chronic abdominal pain or headache. Constipation was common and in some cases there was proteinuria. Systolic murmurs were heard in half the cases, this incidence being higher "than is generally found in healthy children". Pigmentation of the face was noted in one case, and in one a fallacious diagnosis of psychoneurosis had been made. Help in diagnosis may be obtained from the laboratory findings, which included leucopenia with marked neutropenia and relative lymphocytosis, a positive response to the serum agglutination test, and a skin reaction to injection of brucellin. In some cases there are no such findings, although the disease is still active, and the condition must be diagnosed from the history and clinical signs. The author points out that a positive response to the agglutination test may be delayed for some weeks; the titre may rise to 1:80 or higher after a skin test, but this is not always the case.

Treatment with a combination of chlortetracycline and streptomycin is usually rapidly successful, but relapses may occur. Mortality is very low. Prophylaxis depends upon eradicating the disease from cattle. This can be achieved by inoculation of calves with an attenuated vaccine of *Brucella* Strain 19, but since it will be many years before all cattle are protected, pasteurization of all milk is necessary in the meantime. The author emphasizes that milk which has been tuberculin-tested only is not safe.

H. Stanley Banks

43. **Tetracycline in the Treatment of Scarlet Fever.** [In English]
E. KLEMOLA, P. FORSSELL, A. BACKMAN, and N. OKER-BLOM. *Annales paediatriae Fenniae* [*Ann. Paediat. Fenn.*] **3**, 27–36, 1957. 5 figs., 9 refs.

Tuberculosis

44. **Tuberculosis in Children and Adolescents. A Five- to Fifteen Year Follow-up of 105 Patients**
S. COHEN. *Diseases of the Chest* [*Dis. Chest*] **31**, 207–214, Feb., 1957.

In the 10-year period between 1939–1948 inclusive, there were 110 admissions at the Pollak Hospital [Jersey City, U.S.A.] through the age of 15 years for tuberculosis. This study is based on 105 (95·4%) patients in whom clinical information was available 5 to 15 years after their first entrance into the hospital. These cases are classified. Of the group of 55 (52·3% of the total) with primary infection (parenchymal and/or glandular components), 47 (85·4%) are alive and well 5 to 15 years later. The remainder (14·6%) died from hematogenous complications (miliary and meningeal) in the pre-antibiotic era. Of the group of 47 (44·8%) with re-infection pulmonary disease, 32 (68%) are living 5 to 15 years later (up to January 1, 1954) and all but 2 are inactive. Fifteen (32%) in this group died; 12 from progressive pulmonary tuberculosis and 3 from tuberculous meningitis. The re-admission rate was 40% compared to 7·4% for the first infection cases. The remaining 3 (all living) had extra-pulmonary tuberculous foci without roentgen evidence of thoracic disease.

Prognostic factors in the primary infection and therapeutic measures in the re-infection groups are discussed. The best results in the latter patients were obtained with the use of bed rest and artificial pneumothorax.—[Author's summary.]

45. **Benign Idiopathic Spontaneous Pneumothorax in Relation to Tuberculosis.** (Le pneumothorax spontané idiopathique bénin. Ses rapports avec la tuberculose)
A. P. JARNIOU, A. MOREAU, P. BOURDET, and G. LORRIOT. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **20**, 909–937, Sept.–Oct., 1956 [received Feb., 1957]. Bibliography.

During a period of 5 years the authors, working at the Hôpital Militaire Percy, Paris, have found tuberculosis to be the cause in only 2 out of 22 cases of benign spontaneous pneumothorax. From a review of the literature since 1803 [the bibliography occupies no fewer than 9 pages] up to 1955 two facts appear to have been established, namely, the reality and frequency of non-tuberculous spontaneous pneumothorax and the aetiological importance of rupture of subpleural vesicles in the majority of cases.

In the 20 cases of non-tuberculous pneumothorax now reviewed and summarized the ages of the patients ranged between 21 and 35 (average 24); all were males, all were tuberculin-positive, and none had a history of broncho-pulmonary disease. Examination was carried out by means of tomography, pleuroscopy, and biopsy. The authors' hypothesis is that in many cases the so-called idiopathic benign pneumothorax may be connected with a very limited bacillary infection, scarcely visible by radiography and of rapidly favourable development, the only manifestation being the sudden appearance of the pneumothorax.

Treatment followed closely the lines recommended some years ago by Bernard and Meyer (*Dis. Chest*, 1951, **19**, 641). It is not thought that the administration of drugs such as aureomycin is more effective than the technique of inserting talc intrapleurally, which procedure the authors complete by the intrapleural injection of 10 ml. of the patient's own blood. Subsequent chest radiographs are stated to have shown a completely normal picture. In addition they suggest that there may be a place for thoracotomy in certain cases which do not respond to the classic treatment.

The authors conclude by emphasizing that tuberculosis should continue to retain in connexion with spontaneous idiopathic pneumothorax in young subjects the important place it formerly occupied in the aetiology of spontaneous pneumothorax.

Norman F. Smith

46. **The Drug Treatment of Nonhospitalized Patients with Tuberculosis**
A. B. ROBINS, H. ABELES, A. D. CHAVES, M. H. ARONSOHN, J. BREUER, and D. WIDELOCK. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **75**, 41–52, Jan., 1957. 6 refs.

During the 12 months ending July, 1954, at the chest clinics of the New York City Department of Health, 1,646 tuberculous out-patients were given isoniazid, streptomycin, and PAS in differing combinations, and the results obtained in 1,146 who received this treatment for 4 months or more are analysed in this paper. Only 232 of the patients had not previously been in hospital. All patients were advised to rest as much as possible. At the end of 12 months 56% of the patients who had a positive sputum initially were sputum-negative, and for the group of patients who had not previously received chemotherapy this figure was actually 76%. However, isoniazid-resistant strains of bacilli were recovered from 15% of a group of 334 patients in whom the organism was susceptible before treatment started. Radiological improvement was observed in almost half the patients, but in 12% it was found that the *x*-ray appearances had deteriorated.

The best results were obtained, as expected, in the younger age group with minimal lesions and in those with disease of fairly recent onset. At the end of 24 months, 58% of 351 patients who had received 18 months' treatment showed sputum conversion and 47% radiological improvement. This group, however, included a higher proportion of older patients and patients in whom the disease was relatively long-standing. The authors do not consider that domiciliary chemotherapy

has interfered with acceptance by the patients of hospital treatment or contributed to the spread of drug-resistant organisms in the community. *Paul B. Woolley*

47. **Observations on High-dosage Isoniazid Therapy in Tuberculosis in Adolescents.** (Osservazioni sulla terapia isoniazidica ad alte dosi nella tubercolosi dell'adolescenza)
A. Omodei-Zorini, L. Praloran, D. Oricchio, F. Bagnoli, and P. Bonoli. *Annali dell'Istituto "Carlo Forlanini"* [*Ann. Ist. "Carlo Forlanini"*] **16**, 139–159, 1956. 20 figs., 12 refs.

From the Carlo Forlanini Institute, Rome, the authors report the results of treatment with isoniazid alone in high dosage in 20 cases of pulmonary tuberculosis. The patients were aged between 12 and 20 years; 9 had primary lesions in the lung and 11 post-primary lesions. Isoniazid was given in a dosage of 10 mg. per kg. body weight, increasing slowly to 20 mg. per kg. over a period of about 150 days; in no case was more than 1 g. a day given.

Two patients, both with previous evidence of hepatic disturbance and with advanced pulmonary lesions, developed jaundice, but recovered. There were no other toxic effects. In 7 patients with recent and exudative lesions there was complete resolution, often within 3 months. In the remainder, with older lesions, there was for the most part little or no improvement. Only 5 cases were initially sputum-positive, and 3 of these became negative; from one of the patients who remained sputum-positive organisms resistant to more than 100 μg. of isoniazid [? per ml.] were isolated. There was an increase in weight and a fall in the erythrocyte sedimentation rate in most cases. [These are not defined further.]

[Some of the illustrations of successfully treated cases are impressive, but in the absence of a control group it is impossible to come to any definite conclusion.]

Arnold Pines

48. **Minimal Pulmonary Tuberculosis in Military Personnel: World War II**
J. J. Waring and W. H. Roper. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **75**, 1–40, Jan., 1957. 23 refs.

A study is reported of the progress of patients in whom minimal active and inactive tuberculosis became apparent under the most varied environmental conditions, from sedentary occupations to the physical strain of active warfare. In some 95% of the patients studied nothing abnormal was found on the chest radiographs taken on entry to the Services; it is stated that those in whom there was evidence of minimal, healed disease were generally recruited. The cases were collected over a period of 2½ years ending June, 1946, before the introduction of chemotherapy, and all were followed up for a minimum of 3 years.

Of 967 patients studied, 625 were considered to have active and 342 inactive disease. Of those with active disease, 66% deteriorated during the observation period, whereas of those with inactive disease, 78% remained well. In the majority of the patients with active disease some time before recruitment there was a relapse while on service. The probability of relapse was greatest in those with a history of pleural effusion, extrathoracic disease, or less than 6 months of rest. At the end of the observation period 59% of the patients in the active group were alive and well, the corresponding figure in the inactive group being 77%. The authors consider that subjects with a previous history of active pulmonary tuberculosis should not be recruited, that tuberculin-negative reactors should be tested frequently while in the Services, and that serial chest radiographs should be taken in all cases in which sputum conversion is of recent occurrence. *Paul B. Woolley*

49. **Surgery in the Treatment of Pulmonary Tuberculosis in Patients Aged 50 and Over**
A. Pines and R. Rowlandson. *Thorax* [*Thorax*] **11**, 328–333, Dec., 1956. 34 refs.

The results of surgical treatment of pulmonary tuberculosis in patients over 50 were assessed from the case notes, radiographs, and follow-up reports of 120 patients subjected to surgery between 1947 and 1954 at the London Chest Hospital (110) and the London Hospital (10). The mortality rate within 6 months of operation was 7%, and, as expected, the common factor in these deaths was preoperative dyspnoea; none of the patients without this symptom died within 6 months of operation. Similarly, the complication rate was closely related to the presence before operation of dyspnoea and bronchitis. Of the 120 patients, 102 were traced and followed up for periods varying from 6 months to 8 years. Of these, 75 were well (61 being able to work), 22 were unfit, and 5 had died; 86 were sputum-negative.

In the majority of the cases thoracoplasty was performed, and the authors consider that even better results could be obtained with wider use of resection. It is concluded that in this age group satisfactory results can be achieved with surgery, particularly in patients without dyspnoea on exertion or bronchitis.

A. M. Macarthur

EXTRA-RESPIRATORY TUBERCULOSIS

50. **Tubercles of the Choroid**
R. S. Illingworth and J. Lorber. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 467–469, Dec., 1956. 4 figs., 8 refs.

From the University of Sheffield the authors report their findings regarding the incidence and natural history of tubercles of the choroid in 224 cases of miliary and meningeal tuberculosis seen at Sheffield between January, 1947, and January, 1956. Choroidal tubercles were found in a total of 86 (38·4%) of the 224 cases; they occurred in 16 out of 125 children with tuberculous meningitis without radiological evidence of miliary tuberculosis, and in 70 out of 99 with radiological evidence of miliary tuberculosis, with or without meningitis.

The optic fundi of all survivors were repeatedly examined, the longest period of follow-up of the choroidal lesions being 8½ years. In the earliest stage the tubercles

appear as rounded, yellowish areas, paler than the surrounding choroid and merging imperceptibly into it; there may be only one or as many as 10 or 20 in each eye and they are usually situated near the disk. In the second stage the outline becomes sharper, and fine dots of pigment appear in the pale area. Either of these stages, or both, may be present when the child is first seen. The smaller tubercles may remain in this second stage unchanged for years, or may even disappear altogether. However, the larger tubercles, in the course of the next 12 weeks or more, become parchment-white, with a clearly demarcated margin surrounded by heavy black pigment (the 3rd stage) and there may also be some pallor of the surrounding choroid. The last and 4th stage—now described for the first time—is seen only after 3 or 4 years; in this stage the parchment-white area mentioned above is completely replaced by a mass of heavy black pigment.

Choroidal tubercles may occur in the absence of miliary tuberculosis, but although the authors searched for them in over 200 cases of apparently uncomplicated primary tuberculosis, mostly in children under the age of 2, none were found. *B. Golberg*

51. **Intrathecal Hydrocortisone in the Treatment of Tuberculous Meningitis**

C. Choremis, C. Papadatos, A. Gargoulas, and C. Drosos. *Journal of Pediatrics* [*J. Pediat.*] **50**, 138–144, Feb., 1957. 7 refs.

This paper reports the results in three consecutive series of children (82 in all) under treatment for tuberculous meningitis at St. Sophia's Children's Hospital, Athens.

(1) The first group of 24, which included 11 with advanced disease and 6 patients under 2 years of age, received intramuscular and intrathecal streptomycin and isoniazid; in this group 4 patients (3 of them infants) died and one of the 20 survivors has hydrocephalus. (2) The next 29 patients were given the same treatment plus intramuscular cortisone in doses of 25 to 75 mg. daily for 20 to 25 days, 14 having advanced disease and 14 being under 2 years of age; in this group 5 died, of whom 3 were infants, one of the deaths being due to multiple pulmonary staphylococcal abscesses and empyema. One survivor is a decerebrate idiot, while another developed *Haemophilus influenzae* meningitis while under treatment and made a "stormy but uneventful recovery". (3) The last 29 patients, including 10 advanced cases and 8 under 2 years of age, did not receive intrathecal streptomycin, but continued to receive intrathecal isoniazid and were also given 5 mg. of hydrocortisone intrathecally for approximately 3 weeks; here there were 4 deaths (one infant) and 5 patients were still in hospital at the time of reporting. Two of the deaths occurred 3 months after admission to hospital.

Clinical improvement and the return of the cerebrospinal fluid and of the electroencephalographic pattern to normal were quickest in those treated with cortisone. Spinal blocks were not encountered in any of the three groups. The total duration of the different forms of treatment is not stated, but those treated with cortisone were kept in hospital for a shorter period than those who had no cortisone. There were no untoward reactions to intrathecal hydrocortisone, but the danger of intercurrent infections is real (as witness the 2 cases in the second group) and it is suggested that appropriate antibiotics must be given concurrently while the patient is receiving intramuscular or intrathecal cortisone.

[The three groups were roughly comparable, although the investigation was not a controlled one. There was no difference in the mortality rate in the three groups, but one of the deaths might not have occurred without cortisone treatment. The rapid clinical improvement in the cortisone-treated cases led to a radical shortening of the treatment. The long-term effect of this is not apparent, as there is no mention of follow-up after discharge. In the abstracter's view a case for routine cortisone treatment in tuberculous meningitis has not been made out.] *John Lorber*

52. **Clinicopathologic Study of Tuberculous Meningitis in Adults**

H. E. Riggs, C. Rupp, and H. Ray. *American Review of Tuberculosis and Pulmonary Diseases* [*Amer. Rev. Tuberc.*] **74**, 830–834, Dec., 1956. 4 refs.

An analysis of the findings at necropsy at the Philadelphia General Hospital on 3,549 patients with active tuberculosis revealed the presence of tuberculous meningitis in 19·3% of those under 20 years of age and 5·9% of those over this age. The clinical and pathological features in the latter group of 185 patients (mostly negroes) are discussed in the present paper. Meningitis was a terminal feature in one-quarter of the cases. Commonly there was considerable delay in diagnosis, 40 patients being in coma on admission. At least one-third of the group had noted premonitory symptoms, such as headache, neck pain, and vomiting, 1 to 3 weeks before admission. At necropsy active extrameningeal tuberculosis was present in 86%, including miliary tuberculosis in 61%. In 6 cases the origin of the meningeal infection was not determined. The brain was more frequently the site of chronic tuberculous lesions than any other organ except the lung. It is of interest that cerebral tuberculomata were found in 36% of the adults and in only 20% of children. Tuberculomata were often multiple and no part of the central nervous system was entirely spared.

Since active tuberculous lesions are widespread all over the body in patients with meningitis, the authors consider that the cure of meningeal complications in adults may depend primarily upon the control of the spread of the disease before meningeal infection develops.

John Lorber

53. **Hormone Therapy Combined with Antibiotics in the Treatment of Tuberculous Meningitis in Children.** (L'hormonothérapie associée aux antibiotiques dans le traitement de la méningite tuberculeuse de l'enfant)

J. Chaptal, R. Jean, C. Campo, and D. Abram-Dossa. *Pédiatrie* [*Pédiatrie*] **11**, 663–686, 1956.

Venereal Diseases

54. **A Study of Penicillin and Streptomycin in the Treatment of Acute Gonorrhoea and an Analysis of the Incubation Period.** [In English]
A. LODIN. *Acta dermato-venereologica* [*Acta derm.-venereol. (Stockh.)*] **36**, 502–508, 1956. 2 figs., 24 refs.

In a therapeutic trial at Karolinska Hospital, Stockholm, patients with acute gonorrhoea were given a single intramuscular injection of either 0·3 mega unit of penicillin or 0·5 g. of streptomycin, 78 patients receiving penicillin and 76 streptomycin. The patients were Service recruits aged 19 to 21 years. Tests of cure, which included culture of smear, were carried out once a week for 4 to 5 weeks. There was one relapse in each treatment group, but a single repeat injection of the same drug achieved a cure in both instances. The mean incubation period for the series was 6·1 days, the shortest period being a matter of hours and the longest 40 days.
G. L. M. McElligott

55. ***Trichomonas vaginalis* in Urethritis of the Male**
L. G. FEO, N. R. VARANO, and T. R. FETTER. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **32**, 233–235, Dec., 1956. 23 refs.

The part played by *Trichomonas vaginalis* in the aetiology of non-gonococcal urethritis was studied in 183 cases of urethral discharge in males seen at the Urology Clinic of the Jefferson Medical College Hospital, Philadelphia, over a recent 2-year period. All the patients were ambulant, but the group was selected to the extent that patients with other concurrent urinary tract diseases were excluded. A Gram-stained smear of the urethral discharge and a moist-slide preparation were examined for organisms, and on the findings the patients were divided into two main groups—108 with gonorrhoea and 75 with non-gonococcal urethritis. *T. vaginalis* was found in 33 patients, 12 of whom had harboured the organism persistently in spite of treatment for 3 to 20 months, the incidence being 18% of cases of urethral discharge and 41% of the non-specific cases. *T. vaginalis* was found in association with the gonococcus in only 2 cases. Of the 33 patients harbouring *T. vaginalis*, 31 were negroes. Of interest and some significance was the finding that the incidence of infection was high in married men.

Clinically, the incubation period was 1 to 3 weeks. The discharge was typical—namely, a thin mucoid "morning drop" accompanied by slight urethral irritation and discomfort; this persisted in spite of every type of treatment for 6 to 20 months in 7 of the 75 cases of non-gonococcal urethritis.

It is considered that in these cases *T. vaginalis* was the sole aetiological factor. The authors emphasize the limitations of present therapeutic methods; they consider that until a drug is available which will eliminate the organism treatment should be directed towards reassuring the patient before psychological trauma develops.

[A noteworthy feature was the high incidence (18%) of *T. vaginalis*—a much higher incidence than is usual in Britain.] *A. J. Gill*

56. **Furacin Urethral Suppositories in the Treatment of Chronic Non-gonococcal Urethritis**
R. R. WILLCOX. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **32**, 246–250, Dec., 1956.

The author reports the treatment at St. Mary's Hospital, London, of chronic non-gonococcal urethritis in 16 males by means of urethral suppositories containing 0·2% of nitrofurazone together with a local analgesic in a water-dispersible base, as an alternative to the usual treatment with urethral irrigations in cases not responding to antibiotics. The pessaries were inserted twice daily and were well tolerated by all but 2 of the patients, but it was reported by most of the patients that they did not dissolve easily or completely.

There was an immediate improvement in 12 out of 16 cases, but recurrence was recorded in 7. In 2 cases of trichomonal urethritis immediate improvement was noted; the ultimate result could not be assessed in one of these, but in the other a relapse occurred after 9 weeks, with equally striking response to re-treatment. While "no strong curative claims can be made", the method is advocated as a potentially useful alternative to irrigation of the urethra, especially in private practice.

[The results here reported do not seem to present a notable advance in treatment, though other medicaments used in a similar way might prove helpful. There are obvious objections to permitting the patient to insert substances into the urethra.] *Robert Lees*

SYPHILIS

57. **The Use of Whole *Treponema pallidum* (Nicols Strain) in a Complement Fixation Test for the Diagnosis of Syphilis**
H. A. COHEN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **27**, 369–376, Nov., 1956. 16 refs.

Many workers have tried to find a substitute for the technically difficult treponemal immobilization (T.P.I.) test for syphilis. This paper describes a treponemal complement-fixation (T.C.F.) test devised and carried out at the Hebrew University–Hadassah Medical School, Jerusalem, by the Kolmer technique, using half the standard volumes of reagents. The antigen used was a suspension of the Nichols strain of *Treponema pallidum* in 0·25% phenol-saline containing 10 to 15 organisms per high dry field.

The test was performed on 49 sera on which the T.P.I. test had already been carried out. The T.C.F. test gave

positive or doubtful reactions on 29 out of 30 sera from syphilitic patients whose T.P.I. reactions were all positive, but was negative in one case, a patient with treated latent syphilis. Negative T.C.F. test results were obtained on all but one of 19 non-syphilitic patients with negative T.P.I. test results. [In the exceptional case the T.P.I. test result bordered on the doubtful range of immobilization.] In tests on a further 26 syphilitic sera the T.C.F. test was more sensitive than the Kolmer test and gave higher titres in quantitative tests. Sera from 25 patients with a variety of skin diseases were examined; all gave negative Kolmer reactions, but 8 gave positive T.C.F. reactions, the remainder being negative. After absorption of the positive sera with rabbit erythrocytes the T.C.F. reactions became negative, but it was shown that this procedure did not influence positive T.C.F. reactions with syphilitic sera. As non-specific reactions occur with this test, it may be necessary to absorb sera with lipid antigen before testing.

The author suggests that the antibody detected by the T.C.F. test is similar to, if not identical with, the immobilizing antibody.

[It is surprising that such a weak suspension of treponemes should be such a good complement-fixing antigen.] *A. E. Wilkinson*

58. **Catamnestic Investigations in Congenital Syphilis.** (Katamnestische Untersuchungen bei Lues connatalis)
H. Möbest and K. Schmidt. *Ärztliche Wochenschrift* [*Ärztl. Wschr.*] **12**, 34–38, Jan. 11, 1957. 2 figs., 24 refs.

At the Institute of Hygiene of the University of Kiel 4,837 antenatal specimens of serum have been tested for syphilis since November, 1953, by means of the treponemal immobilization test in addition to the classic reactions. In 101 cases (2·06%) the results were positive, and of the children born, 18 (0·37%) were seropositive at birth. Intensive family investigations in these cases have since resulted in the discovery of further untreated cases of syphilis. The authors draw attention to the fact, reported by various authors, that whereas the incidence of acquired syphilis has apparently decreased substantially during the last 10 years, that of congenital syphilis has decreased more slowly. In order to improve this state of affairs it is suggested that more widespread use of the routine antenatal blood test should be made, and that maternity benefits under social security schemes should be made conditional on the patients undergoing three such tests during pregnancy, the first preferably in the second month. *G. W. Csonka*

59. **The Use of Vegetable Antigens in Serological Tests for Syphilis.** (Антигены из растительных веществ для серологических реакций на сифилис)
L. C. Reznikova. *Вестник Венерологии и Дерматологии* [*Vestn. Vener. Derm.*] 43–45, No. 6, Nov.–Dec., 1956 [received Feb., 1957].

The antigens which are most commonly employed for serological reactions in the diagnosis of syphilis are usually prepared from beef heart and the active part of the antigen includes phospholipids and lecithins activated by cholesterol. This paper describes attempts made at the Central Dermato-Venereological Institute, Moscow, to produce antigens from vegetable sources, tests being made with such substances as soya flour, wheat and potato flour, almonds, arachis, and walnuts. It was established that phospholipids are indeed present in those substances, but in lesser amount than in animal muscle, and that lecithin is entirely absent. The technique of the extraction of phospholipids is described.

As a result of the study antigens were prepared consisting of one part of phospholipid (extracted from plants), 2·5 parts of lecithin (extracted from beef heart), and 15 parts of 1% solution of cholesterol. These antigens were used in carrying out the Wassermann test (in parallel with the usual antigens) and showed high sensitivity. In testing 1,410 sera with antigen from soya flour results identical with those by the usual method were obtained in 97·88% of cases. With almond antigen the results agreed in 98·38% of 740 sera tested, but with potato-flour antigen agreement was achieved in only 90·7%. *H. Makowska*

60. **Late Results of Fever Therapy in Neurosyphilis.** [In English]
H. Kopp and W. Raaschou-Nielsen. *Acta dermato-venereologica* [*Acta derm.-venereol.* (*Stockh.*)] **36**, 482–501, 1956. 25 refs.

An analysis is reported from Rigshospitalet, Copenhagen, of the results of treatment of neurosyphilis over the period 1937–52. Of 277 patients (166 males and 111 females), 183 were given fever therapy (induced by injection of *Escherichia coli* vaccine), 67 received fever therapy with penicillin, and 27 were given penicillin only. It is stated that " as an adjuvant to fever therapy injections of arsenic and bismuth were given throughout the period in the commonly employed dosages ".

[The analysis is exhaustive and not suitable for abstracting, but the following points from the authors' conclusions are of particular interest.] In 88% of 150 patients the spinal fluid was inactive after treatment. In 11 out of 18 patients with optic-nerve atrophy there was no further progression of visual disturbances. Recurrences were seen only in patients with severe neurosyphilis and did not appear to be related to " the number of fever attacks reaching 40° C." There were no recurrences in patients in whom fever was induced by means of the "hypertherm". The addition of arsenic and bismuth to the treatment regimen did not ensure continued negativity of the serum or spinal fluid. In 50 of the 65 patients who died before the time of follow-up, death was due to causes other than neurosyphilis. Mortality from fever therapy was 2%. The duration of symptoms before treatment was a valuable prognostic factor; 27 out of 43 patients admitted within 6 months of the onset of symptoms were cured or improved, compared with 42 out of 105 who had symptoms for more than 6 months. *G. L. M. McElligott*

61. **Syphilis Morbidity Reporting by Private Physicians**
E. E. Taylor and J. J. Wright. *Public Health Reports* [*Publ. Hlth Rep.* (*Wash.*)] **72**, 85–93, Jan., 1957. 7 refs.

Tropical Medicine

62. **Experimental *Entamoeba histolytica* Infections in Man**

P. C. BEAVER, R. C. JUNG, H. J. SHERMAN, T. R. READ, and T. A. ROBINSON. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **5**, 1000–1009, Nov., 1956 [received Feb., 1957]. 17 refs.

In a study of the susceptibility to infection with *Entamoeba histolytica* and the stability of such infection, carried out at Tulane University School of Medicine, New Orleans, cysts of *E. histolytica* were administered to 130 white and negro volunteers from among the prison inmates of a State penitentiary in Mississippi. The cysts were obtained directly from a non-symptomatic carrier or after passage through other volunteers and ingested in a carbonated beverage; the stools of the volunteer subjects were examined once before inoculation and only those without signs of *E. histolytica* infection were admitted to the experiment.

All of 42 individuals ingesting 2,000 to 4,000 cysts were infected, while larger inocula (containing 10,000 to 1,000,000 cysts) produced infections in 4 others. All but 2 of the infections were detected within 14 days, although one infection was not detected until 4 months after inoculation, but this was exceptional. Out of 23 infected prisoners observed for 9 to 14 months, 7 spontaneously lost their infection. Of these 7 individuals, 3 were given further doses of cysts (4,000); 2 were again infected, but one was refractory to re-infection. None of the subjects developed clinical symptoms of amoebiasis, but as some amoebic lesions were found in experimentally infected dogs, guinea-pigs, and rats, the authors consider that the strain could not be regarded as non-pathogenic. *R. A. Neal*

63. **Experimental Chemoprophylaxis of Amebiasis**

P. C. BEAVER, R. C. JUNG, H. J. SHERMAN, T. R. READ, and T. A. ROBINSON. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **5**, 1015–1021, Nov., 1956 [received Feb., 1957]. 18 refs.

At Tulane University School of Medicine, New Orleans, the value of chemoprophylaxis against amoebiasis was studied experimentally by administering various drugs to a series of prisoner volunteers and then challenging them with cysts of *Entamoeba histolytica* obtained from a carrier and ingested in a beverage. The drugs used were "milibis" (bismuth glycollylarsanilate) in doses of 500, 250, 150, and 75 mg. once a day for 28 days and then 250 mg. once a day for 21 days; "diodoquin" (di-iodohydroxyquinoline) in doses of 650, 325, and 210 mg. daily for 21 days; "atabrine" (mepacrine), 500 mg. daily for 2 days, then 100 mg. daily for 21 days; and chloroquine, 500 mg. daily for 3 days, then 500 mg. once a week for 3 weeks; control subjects were given 330 mg. of sodium bicarbonate. The volunteers were divided into groups of 8 for each dose level, with 8 controls. In the case of the 28-day experiments challenges were given at the end of the 1st, 2nd, and 3rd weeks, and in the 21-day experiments at the end of the 1st and 2nd weeks.

It was found that 250 and 500 mg. of milibis daily for 28 days and 650 mg. of diodoquin daily for 21 days protected all individuals from infection with *E. histolytica*, any lower doses of the drugs failing to give complete protection. A further trial with 250 mg. of milibis daily for 21 days protected 13 out of 14 subjects from infection; it was thought that the one infected individual may not have swallowed all the drug, since his infection disappeared when the same dosage of the drug was later administered under special supervision. Mepacrine and chloroquine failed to show any prophylactic action. All control subjects became infected, generally within the first week. *R. A. Neal*

64. **Four Years' Experience of Melarsen Oxide/BAL in the Treatment of Late-stage Rhodesian Sleeping Sickness**

F. I. C. APTED. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **51**, 75–86, Jan., 1957. 32 refs.

The author presents the results of 4½ years' experience in the treatment of late-stage *Trypanosoma rhodesiense* infections in man in Tanganyika with a combination of melarsen oxide and BAL ("mel B", "arsobal"). The paper contains case histories and also describes various dosage schedules [but for these the original should be consulted]. Of 176 patients treated, just over 10% (18) died of the disease or its treatment; but all the deaths occurred in patients who were in extremely poor condition or almost moribund when first seen. One death was certainly due to treatment after what, in the light of later experience, would now be regarded as a rather incautious dosage in a patient already far beyond normal drug treatment; 3 other deaths were possibly due to the drug rather than to the disease, while the remaining patients failed to respond to treatment. Altogether 18 patients relapsed after the first course, but of these 12 responded to further treatment; in 5 of these cases the initial dosage was known to be inadequate, and a further 3 patients proved to be resistant to treatment.

The drug is given as a 3·6% solution in propylene glycol, 5 ml. of this solution given to a patient weighing 50 kg. therefore representing a dose of 3·6 mg. per kg. It is recommended that the full course of treatment should be at least 25 or 30 ml. and that this be given whether the patient is in the intermediate or the advanced stage of the disease. The best results were obtained from a double course, consisting in 3 injections followed by a rest period of 2 weeks and then a further 3 injections. The author states that even patients in very poor condition can be brought round and apparently cured by careful individual treatment, particularly in regard to dosage, aided by good nursing. It is considered that, provided due assessment is made of the patient's con-

dition before treatment and that careful watch is kept on his response, the dosage being regulated accordingly, the compound is valuable and safe. A notable feature in this series was the often " astonishing " improvement in the patient's mental state. *I. M. Rollo*

65. Treatment of Blackwater Fever with Prednisone

H. C. TROWELL and J. M. VAIZEY. *Lancet* [*Lancet*] 2, 1281–1282, Dec. 22, 1956. 5 refs.

Prednisone was administered in 5 uncomplicated cases of blackwater fever in 3 Africans, aged 60, 6, and 1½ years respectively, and 2 Asians aged 40 and 23 years respectively. The oldest African had had an abdominal operation and blood transfusion 3 days before haemoglobinuria developed, but the authors regard this interval as too long for the appearance of the effects of incompatible transfusion. The drug was given to the adults in doses of 40 to 150 mg. spread out over one to 7 days. The infant received 20 mg. on the morning and evening of one day.

Clinical response was rapid, and pigments disappeared from the urine within a few days. The authors recommend the use of prednisone or cortisone in the treatment of all cases of blackwater fever. *B. G. Maegraith*

66. The Intensive Treatment of Urinary Schistosomiasis with Trivalent Sodium Antimony Gluconate

H. A. K. ROWLAND. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **50**, 565–575, Nov., 1956. 5 refs.

The results of a clinical trial of trivalent sodium antimony gluconate (T.S.A.G.) which was carried out at Messina, Northern Transvaal, on 143 African, 1 " coloured ", and 4 European patients suffering from urinary schistosomiasis are reported. The drug was supplied in the form of a powder, which for use was dissolved in distilled water and given by intravenous infusion within 20 minutes of preparation. In 5 cases in which a small quantity of solution was accidentally given extravenously, pain produced at the site subsided quickly upon application of a fomentation. The series was divided into 6 groups, each with different programmes of treatment over periods ranging from 8 hours to 5 days. Follow-up examinations were carried out on specimens of urine during and after completion of treatment, and then at intervals of one month or less, for a period of 6 months, at which time 3 consecutive daily specimens of urine were examined, a rectal biopsy was carried out, and all urinary sediments were subjected to hatching tests for ova. The criteria of cure were the absence of viable ova in the urine or in rectal biopsy material and negative results of hatching tests.

The results in the six treatment groups were as follows. (1) These 25 patients received 6 consecutive daily injections of 225 mg. of T.S.A.G. (total 1,350 mg.). Side-effects were almost completely absent and in no case had treatment to be abandoned because of undesirable reactions. At the end of 6 months 19 patients presented for examination and of these, 2 were showing viable ova and 5 non-viable ova. Of those patients who underwent the full course of treatment, 83·3% were cured. (2) These 24 patients received the same total dose of T.S.A.G. as those in Group 1, but given in doses of 337·5 mg. daily for 4 days. No side-effects occurred in 12 cases, while in the remaining 12 the chief complaints were headache, cough, substernal pain, vomiting, epigastric pain, and fever; but no patient complained of more than one side-effect after any injection and no course of treatment was abandoned. Of the 11 patients who came for examination at 6 months, none showed any viable or non-viable ova, an estimated cure rate of 100%. Up to the 4th month after treatment 5 patients were showing viable (one case) or non-viable (4 cases) ova. (3) The 31 patients in this group were given the same total dosage as before, but divided into doses of 225 mg. twice daily for 3 days. One patient died after the 4th dose, but independent post-mortem findings revealed no evidence that antimony played any part as a cause of death. Side-effects were observed in 14 cases, but no complaint was made by the remaining 17 patients and the course was completed in all but 2 cases. At the 6-month follow-up viable ova were present in 4 and non-viable ova in 2 of the 17 patients presenting for examination, a cure rate of 70·6%. (4) Here the same total dose (1,350 mg.) was given in fractions of 225 mg. three times daily for 2 days. Side-effects were more frequent, being experienced by 24 of the 27 patients in the group, but were not severe enough to cause treatment to be interrupted or abandoned. At 6 months none of the 16 patients who presented were showing viable ova and 4 were showing non-viable ova. [On the author's criteria this represents a 100% cure rate, but the presence of non-viable ova at 6 months in 4 cases leaves this figure open to question.] (5) The same total dose of 1,350 mg. was given to the 19 patients in this group in three separate doses of 450 mg. at 12-hour intervals, each dose being given in 10 ml. of distilled water and injected slowly over a period of 5 minutes. Of the 57 injections given, complaints were received after 35. At the 6-month follow-up viable ova were present in 3 cases and non-viable ova also in 3 of the 16 cases seen, an estimated cure rate of 76·5%. (6) Lastly, 22 patients were given a reduced total dose of 900 mg., either in four injections of 225 mg. over 8 hours or in two injections of 450 mg. at an 8-hour interval. The injections were given slowly over 5 minutes and the patients rested or were in bed overnight between the injections. In the first group (4 injections) side-effects were experienced after 23 of the 47 injections and the course was stopped after the 3rd injection in one case because of vomiting; among those given 2 injections no side-effects were experienced. At the 6-month examination 6 out of 9 patients in the first section were cured (60%) and 3 out of 8 in the second section (37·5%).

The author concludes that in the treatment of schistosomiasis with trivalent sodium antimony gluconate high therapeutic effectiveness need not be associated with high toxicity, but that the more intensive the course, the greater the toxicity; that side-effects are frequent, but usually not severe; that changes in the electrocardiogram and leucocyte count are marked, but return to normal; and that T.S.A.G. is lethal to *Schistosoma haematobium*.

O. D. Standen

Allergy

67. **Conjunctivitis and Eyelid Eczema due to Hypersensitiveness to Adrenalin Solution Employed in Spray-treatment of Asthma.** [In English]
H. COLLDAHL and E. FAGERBERG. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **10**, 77–81, 1956. 8 refs.

Hypersensitivity reactions to adrenaline injections, generally occurring locally in the skin, have been reported in the past. The reaction may occur with adrenaline prepared synthetically or made from animal adrenal tissue. A case occurring in a patient who had been using an adrenaline spray for 9 months for relief of asthma is described. Because of intense conjunctivitis and oedema of the eyelids she was admitted to St. Goran's Hospital, Stockholm. Skin tests with 10% adrenaline solution gave a "strong positive" reaction, while other components of the atomizer gave a negative response. An injection of adrenaline caused local ischaemia at the site of injection, but no response was obtained when other asthmatics were tested with the adrenaline. On discontinuing use of the atomizer the eye changes cleared in a few days. *A. W. Frankland*

68. **Diagnostic Use of Alterations in Eosinophils after Injection of Histamine into Allergic Patients.** [In English]
E. ANDERSSON. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **10**, 246–253, 1956. 1 fig., 10 refs.

The effect of injection of histamine on the eosinophil count in allergic patients was studied at the University Hospital, Copenhagen. In 50 asthmatic patients and 50 healthy controls the eosinophil count was determined before and 15 minutes after subcutaneous injection of 0·5 mg. of histamine. In 44 of the allergic patients there was an increase in the number of circulating eosinophils and in 6 there was a slight fall. Nearly all the patients experienced constitutional reactions, from a feeling of slight pressure in the chest to an actual attack of asthma. In 34 of the controls the eosinophil count fell, in 12 it rose, while in 4 there was no change; none of the controls experienced any reactions. It is suggested that the increase in the eosinophil count may be of diagnostic value in allergic asthma. *A. W. Frankland*

69. **The Detection of Antibodies in Hayfever Sera by Means of Hemagglutination**
R. J. FEINBERG, J. D. DAVISON, and J. A. FLICK. *Journal of Immunology* [*J. Immunol.*] **77**, 279–286, Oct., 1956. 27 refs.

A study was carried out at the University of Pennsylvania to determine whether the reagin type of antibody found in hay-fever serum can be measured by the haemagglutinating technique of Boyden (*J. exp. Med.*, 1951, **93**, 107), in which protein antigens are adsorbed on to tanned human erythrocytes. This technique was used on sera from 30 patients with hay-fever treated by hyposensitization and 37 untreated patients, also on 5 specimens of rabbit immune serum. Precipitation tests and Prausnitz–Küstner tests were also performed on these sera. The haemagglutinating antibody was found to be more often present in the serum of hyposensitized patients than in that of untreated patients. Evidence was obtained, however, that this antibody is not identical with the reagin type of antibody. It is concluded that probably both multivalent- and univalent-acting types of antibody can be measured by the haemagglutinating technique. *P. E. Conen*

70. **Formalinized Pollen Tannate in Desensitization Treatment**
H. L. NATERMAN. *Journal of Allergy* [*J. Allergy*] **28**, 76–83, Jan., 1957. 7 refs.

Most methods hitherto used to increase the safety and effectiveness of parenteral pollen desensitization have depended on prolongation of absorption of the antigen by the addition of oil or gelatin to the menstruum or by changing the physical state of the antigen by precipitation by tannic or hydrochloric acids. Acid precipitation causes very little or no denaturation and such precipitates may still produce potentially dangerous local or general reactions. A method of denaturing such precipitates which would reduce or eliminate immediate reactivity without destroying antigenicity has therefore been sought at the Beth Israel Hospital (Harvard and Tufts Medical Schools), Boston. Pollen antigens prepared in the usual way from short ragweed, timothy and orchard grass, and birch and oak were precipitated by tannic acid and zinc and then treated with formalin in concentrations of 0·25 to 2% for 6 days to 6 months. It was determined that a concentration of 0·5% of formalin was effective in reducing reactivity without destroying antigenicity even on prolonged contact, and this strength was therefore adopted. The formalin was subsequently neutralized with sodium bisulphite, and aluminium hydroxide and hydrocortisone acetate were added (to give final concentrations of 0·25% in each case) to the saline suspension of formalinized pollen tannate. The immediate skin reaction to antigens prepared in this way was shown to be reduced and their absorption prolonged in comparison with standard preparations. In the treatment of 193 pollen-sensitive patients over a period of 2 years, representing 355 tree, grass, or ragweed pollen seasons, these preparations gave satisfactory results, the usual maximum dose of 0·25 mg. N (25,000 protein N units) being reached in 3 injections and the number of injections needed being reduced to about 6 per season. It is pointed out that without controlled studies on a large scale the relative merits of this and other types of antigen for pollen desensitization cannot accurately be assessed, but the author claims that the satisfactory clinical results obtained in this series, which appear to compare favourably with those obtained by other methods of desensitization, indicate that such further studies are warranted. *H. Herxheimer*

Nutrition and Metabolism

71. **A Clinical Study of the Effect of Arginine on Blood Ammonia**

J. S. NAJARIAN and H. A. HARPER. *American Journal of Medicine* [*Amer. J. Med.*] **21**, 832–842, Dec., 1956. 3 figs., 26 refs.

In so far as the cerebral disturbance in liver failure is related to an increase in the blood ammonia level, correction of the latter should lead to improvement in the cerebral condition. In this paper from the University of California School of Medicine, San Francisco, the mechanism whereby arginine intravenously administered lowers the blood ammonia level is discussed and the results of arginine therapy in 15 patients with liver failure are reported. In all cases there was a fall in the blood ammonia level associated with clinical improvement. Moreover, 2 out of 3 patients who were given arginine while in deep coma occurring during acute hepatitis responded in 24 to 36 hours with marked clinical improvement and eventual recovery.

[These results seem more uniform than those obtained more recently with glutamate, and further experience with arginine may define more clearly the relation between ammonia intoxication and hepatic coma.]

D. A. K. Black

72. **Dietary Protein and the Serum Cholesterol Level in Man**

A. KEYS and J. T. ANDERSON. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **5**, 29–34, Jan.–Feb., 1957. 37 refs.

In general, there is a rough relationship between the fat intake and the protein intake of a population. The present authors report a study of the effect on the serum cholesterol level of changes in the protein content of the diet, the subjects being schizophrenic males, aged 32 to 54 years, in the Hastings State Hospital, Hastings, Minnesota.

In one experiment 9 men in a control group and 8 in a study group were given similar diets with a fairly low fat content for a month, the diets providing daily 3,000 Cal., 85 g. of protein, and 55 g. of fat. With the same total number of calories both groups were then given extra butter-fat which raised the fat intake to 125 g. The experimental group also received 135 g. of protein instead of 85 g. by the addition of skimmed milk powder. The changes in the diet resulted in an increase in the serum cholesterol level, the increase being the same in both groups.

In another experiment observations were made on two groups of subjects over 4 dietary periods of 4 weeks each. In both groups 1,000 mg. of cholesterol was added daily to the diet in the second and third dietary periods. Protein intake was also increased by about 65 to 70 g., giving a total of approximately 130 g., in the second 4-week period for one group and in the third 4-week period for the other group. These dietary changes did not cause any significant change in the serum cholesterol level in either group.

A table shows the average proportion of the total calories supplied by fat and by protein in the diets of populations of various countries, and the authors point out that there is much less relationship between these than is usually thought to be the case. It is considered that these results lend no support to the hypothesis that atherosclerosis is associated with "levels of dietary protein". [This conclusion would be more certain if the control levels of protein given to the experimental groups were closer to those of populations with low protein intakes. It is also difficult to be certain of the meaning of dietary levels of fat and protein in different countries when these are quoted in the current fashion in terms of percentage of calories rather than of absolute values.]

John Yudkin

73. **The Use of I^{131} Triolein in the Study of Absorptive Disorders in Man**

P. BERES, J. WENGER, and J. B. KIRSNER. *Gastroenterology* [*Gastroenterology*] **32**, 1–16, Jan., 1957. 10 figs., 19 refs.

In a study of fat absorption and its disorders in man, undertaken at the University of Chicago, the radioactivity of blood, urine, and faeces was estimated after the administration of a test meal containing triolein labelled with 40 to 100 μc. of radioactive iodine (^{131}I). Oxalated whole blood, taken 2, 4, 6, and 8 hours after the meal was treated with 20% trichloracetic acid to precipitate the lipid-bound ^{131}I, the activity of the precipitate determined, and the total circulating lipid ^{131}I calculated from this on the assumption that the blood constitutes 7·7% of the body weight. In 30 normal subjects the circulating lipid ^{131}I reached a peak value of 2 to 8% of the ingested dose in 4 to 6 hours and had fallen to 1 to 5% at 8 hours.

In patients suffering from non-tropical sprue, pancreatic disease, post-gastrectomy steatorrhoea, and steatorrhoea due to intestinal hurry there was good correlation between the absorptive pattern thus determined and the degree of steatorrhoea, low or flat absorption curves being associated with severe steatorrhoea. It was not possible to distinguish between diseases of the biliary tract and pancreatic disease by means of the absorption patterns alone. Poor correlation was obtained between the absorptive pattern and the degree of steatorrhoea in regional enteritis, the pattern being within the lower limits of the normal range even with severe steatorrhoea. The absorptive pattern was found to correlate well with the findings of the vitamin-A absorption test.

Estimation of ^{131}I excretion in 24-hour urine collections was of little value in the differential diagnosis of

steatorrhoea. In 5 normal subjects faecal excretion of ^{131}I did not exceed 1% of the dose in 3 days. In 7 patients with steatorrhoea, however, the faecal excretion of ^{131}I was increased significantly. *M. Lubran*

74. **The Use of I^{131} Labeled Fat in the Study of Fat Digestion and Absorption in Normal Individuals and in Patients with Diseases of Fat Absorption**
R. D. McKenna, R. H. Bourne, and A. Matzko. *Gastroenterology* [*Gastroenterology*] **32**, 17–24, Jan., 1957. 3 figs., 10 refs.

The radioactivity of the blood, faeces, and serum of healthy subjects and of patients with abnormalities of fat absorption was studied at the Royal Victoria Hospital (McGill University), Montreal, following the administration of triolein labelled with 50 or 100 μc. of radioactive iodine (^{131}I). Blood was collected hourly for 6 hours after the dose and at longer intervals subsequently, urine for 24 hours, and stools for 2 or 3 days. In a control group of 15 healthy adults peak serum levels of radioactivity occurred after 3 to 4 hours, except in 2 cases in which the peak was at the 9th hour. In 7 cases 1·1 to 4% of the dose was excreted in the faeces in 3 days, in 5 cases 0·7 to 1·5% was excreted in 2 days, and in 2 cases 0·3 and 0·7% in 24 hours. Urinary excretion of ^{131}I and thyroid uptake of the isotope were very variable.

Serum levels of radioactivity were low in 2 patients with pancreatic carcinoma and 2 patients with idiopathic steatorrhoea. In 3 patients after partial gastrectomy the serum level of ^{131}I showed a rapid rise in the first hour to a plateau, falling after the 6th hour. These patients had steatorrhoea and an increased faecal excretion of ^{131}I. Raised faecal values were also found in 2 patients with regional ileitis, an infant with fibrocystic disease of the pancreas (dose 9 μc.), and 2 patients with post-gastrectomy steatorrhoea. The authors conclude that faecal excretion of ^{131}I is a better indicator of total absorption of labelled fat than the blood content.

M. Lubran

75. **The D-Xylose Absorption in Malabsorption Syndromes**
J. A. Benson, P. J. Culver, S. Ragland, C. M. Jones, G. D. Drummey, and E. Bougas. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 335–339, Feb. 21, 1957. 4 figs., 15 refs.

Because oral tolerance tests with dextrose do not always give satisfactory results in coeliac disease and sprue, the value of performing the test with the pentose D-xylose has been investigated at Massachusetts General Hospital, Boston. After an 8-hour fast 25 g. of D-xylose was given orally in water and the urine collected for the next 5 hours. In 24 healthy subjects an average of 6·5 g. was excreted in the 5 hours, that is, about 25% of the ingested dose, whereas in 28 cases of untreated sprue the excretion of xylose fell to about 1 g. in 5 hours, a significant difference. The urinary excretion of D-xylose was normal in cases of pancreatic steatorrhoea, but was abnormally low in patients after gastric resection and in the presence of disease of the small intestine. The urinary xylose excretion increased in patients with sprue whose condition improved with treatment.

The blood xylose level was also determined for up to 4 hours. In normal subjects the D-xylose tolerance curve showed a peak between one and 2 hours which was followed by a rapid fall, but there was considerable individual variation; in patients with sprue the curves tended to be flatter. However, the results of this determination were much less clear-cut than those of the 5-hour urinary excretion test. It is concluded that the latter is a simple and useful test in the diagnosis of sprue, and also of value in assessing the effect of therapy.

Kenneth Gurling

76. **Previously Undescribed Clinical and Postmortem Observations in Non-tropical Sprue: Possible Role of Prolonged Corticosteroid Therapy**
H. W. Himes, J. B. Gabriel, and D. Adlersberg. *Gastroenterology* [*Gastroenterology*] **32**, 60–71, Jan., 1957. 7 figs., 16 refs.

From the Mount Sinai Hospital, New York, the authors describe a case of presumed primary idiopathic steatorrhoea [no studies were made of the effect of a gluten-free diet] of which the clinical manifestations appeared for the first time in a previously healthy male of 34. Response to low-fat, high-protein diet and haematinics was poor initially. Rectal bleeding occurred after 4 months and episodes of abdominal pain and fever after 8 months and during the next 3 years. Treatment with corticotrophin (ACTH) was started 5 months after the onset of the illness (cortisone being given later) and resulted in marked improvement which was maintained for 2 years, when rectal bleeding recurred. This responded to conservative treatment and temporary withdrawal of cortisone, but massive gastro-intestinal bleeding took place 10 months later while the patient was responding well to further steroid therapy. Subtotal gastrectomy was carried out and 3 weeks later, shortly after cortisone therapy had been started again, there was further bleeding. The patient's condition deteriorated, the steatorrhoea increased, and he became resistant to all therapy, including hydrocortisone and corticotrophin. He died 4 years after the onset of the disease. *X*-ray examination shortly before death showed unusual hypomotility of the small intestine, with atony and dilatation.

At necropsy, in addition to the usual findings of idiopathic steatorrhoea, there was extensive ulceration of the small intestine, with a perforation of the jejunum, and thickening of the mesentery and distension of the lymphatic channels. There was no evidence of any disease known to produce secondary steatorrhoea. The authors state that they are unable to give a definite interpretation of the clinical and pathological findings in this case, which do not fit into any known pattern.

M. Lubran

77. **Failure of *alpha*-Phenylbutyrate and *beta*-Phenylvalerate in Treatment of Hypercholesterolemia**
D. S. Fredrickson and D. Steinberg. *Circulation* [*Circulation* (*N.Y.*)] **15**, 391–396, March, 1957. 1 fig., 13 refs.

Gastroenterology

78. **The Syndrome of Gastroduodenal Disease Associated with Chronic Cor Pulmonale**
Z. PLOTKIN. *Diseases of the Chest* [*Dis. Chest*] **31**, 195–206, Feb., 1957. 3 figs., 11 refs.

The syndrome of gastroduodenal disease associated with chronic cor pulmonale due to bronchitis and emphysema (other causes of cor pulmonale having been excluded) is discussed in this paper from the Veterans Administration Hospital, Whipple, Arizona. There were 65 cases of pulmonary emphysema and chronic cor pulmonale in 414 necropsies performed in the period 1948–55, and in 27 of these there was gastroduodenal disease—gastric ulcer, mostly on the lesser curvature in the prepyloric region, in 10, duodenal ulcer in 11, and hypertrophic gastritis in 6. Death from massive haemorrhage occurred in 7 of the 27 cases and from haemorrhage and perforation in 2; only in 3 cases was the diagnosis established before death.

For purposes of comparison the author studied the findings on *x*-ray examination of the gastroduodenal tract in 65 patients in hospital suffering from pulmonary emphysema and cor pulmonale. It was found that 7 had gastric ulcer, 10 duodenal ulcer, 5 both gastric and duodenal ulceration, and 28 had hypertrophic gastritis. In only a small minority was the presence of gastroduodenal disease suggested by the clinical picture.

In view of the high incidence of peptic ulceration in these cases and the frequency of severe haemorrhage, the author suggests that radiological examination of the gastroduodenal tract should be a routine procedure in all patients suffering from cor pulmonale. He emphasizes the lack of characteristic symptomatology and the value in diagnosis in some cases of the absence of polycythaemia. *J. Warwick Buckler*

79. **Influence of Hydrochloric Acid on Gastric Secretion and Emptying in Patients with Duodenal Ulcer**
J. N. HUNT. *British Medical Journal* [*Brit. med. J.*] **1**, 681–685, March 23, 1957. 3 figs., 22 refs.

One cause of the gastric hyperfunction which occurs in patients with duodenal ulcer may be a failure of the duodenal mechanisms which inhibit gastric activity. In an investigation at Guy's Hospital Medical School, London, of this hypothesis—which embraces both gastric secretion and emptying—the effects were studied of adding 20 mEq. of hydrochloric acid per litre to a test meal of 750 ml. of a solution containing 100 g. of glucose per litre. The test was performed 18 times on 16 patients with uncomplicated active duodenal ulcer, 27 students acting as controls. The meals contained the dye phenol red, which is not absorbed by the gastric mucosa, as an indicator and were given by gastric tube which was left *in situ* for 30 minutes, after which the stomach was emptied. Examination of the aspirate showed the volume of the original meal remaining in the stomach at the time of recovery and the total amounts of acid, chloride, and pepsin secreted; the volume of gastric contents which had passed into the duodenum was also calculated.

The author found no significant difference in the rates of gastric emptying with either of the meals between control subjects and the patients with duodenal ulcer, but the latter secreted twice as much acid, chloride, and pepsin as did the former. The addition of hydrochloric acid to the test meal reduced the output of acid in normal subjects by an average of one-fifth. When the data were expressed in terms of parietal and non-parietal components of gastric secretions, it was shown that the addition of acid to the test meal decreased the mean secretion of the parietal component and increased the output of non-parietal secretions in the normal subjects. In the patients with duodenal ulcer, the addition of acid caused no significant mean change in the values for the constituents of gastric juice; in 6 of the 16 patients there was either a very small fall or an increase in acid secretion.

The place of these findings in the causation of hyperfunction of the stomach in patients with duodenal ulcer is discussed, it being concluded that the failure of duodenal inhibitory mechanisms is only an inconstant and minor factor in such hyperactivity. [See also *Lancet*, 1957, **1**, 132; *Abstracts of World Medicine*, 1957, **21**, 390.] *T. J. Thomson*

80. **The Evaluation of Pancreatic Function by Use of I^{131} Labeled Fat**
W. W. SHINGLETON, G. J. BAYLIN, J. K. ISLEY, A. P. SANDERS, and J. M. RUFFIN. *Gastroenterology* [*Gastroenterology*] **32**, 28–32, Jan., 1957. 6 refs.

In investigations carried out at the Veterans Administration Hospital and Duke University, Durham, N. Carolina, patients with pancreatic disease were given 50 or 100 μc. of triolein labelled with radioactive iodine (^{131}I) and blood taken 4, 5, and 6 hours later. Radioactivity of whole blood was determined and also the activity of stools collected for 48 hours after the dose.

In 24 normal control subjects the mean faecal excretion of ^{131}I was 0·6% of the dose (S.D. 0·4%). Of 8 patients with chronic pancreatitis faecal excretion varied from 13 to 61% in 7 and was 0·4% in the 8th. Of 10 patients with pancreatic carcinoma, excretion varied from 12·9 to 93·7% in 8 and was 0·5% and 1·9% respectively in the others.

Blood levels were expressed as the sum of the 4-, 5-, and 6-hour values. In 25 normal subjects the mean was 40·3% (S.D. 9·3%) of the dose. In 9 of 12 patients with pancreatitis it was less than 11%, and it did not exceed 40·3% in the others. In 18 patients with carcinoma of the pancreas low blood values were also found, none exceeding 31·7%. *M. Lubran*

LIVER AND GALL-BLADDER

81. **The Rare Occurrence of Metastatic Carcinoma in the Cirrhotic Liver**

M. M. LIEBER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 145–152, Feb., 1957. 11 refs.

The author attempts to show that metastatic carcinoma rarely occurs in the liver with portal cirrhosis, and for this purpose analyses the findings at 24,329 necropsies performed at the Philadelphia General Hospital (Group 1) and 5,450 performed at the Jefferson Medical College Hospital, Philadelphia (Group 2). Cirrhosis of the liver was found in 3·12% of Group 1 and carcinoma in 15·72%; both conditions were found in 2·16%. The figures for Group 2 were 5·74%, 23·2%, and 4·3% respectively. The incidence of cirrhosis of the liver in patients with carcinoma was about 70% of the incidence in the general population, owing in part to the different age groups tending to be affected.

Metastatic carcinoma of the liver without portal cirrhosis was frequent—28·6% of all carcinomata. Metastatic carcinoma in a liver with portal cirrhosis was observed in only one case in Group 1 and 5 cases in Group 2—an over-all incidence of 0·12% of all carcinomata. The metabolic and other factors considered to be responsible for this low incidence included the increase in portacaval shunt due to deranged liver circulation, reduction in the vascular bed, and the increased fibrous tissue of the cirrhotic liver. *J. B. Cavanagh*

82. **Cirrhosis and Primary Carcinoma of the Liver. Changes in Their Occurrence at the Boston City Hospital, 1897–1954**

R. A. MACDONALD. *New England Journal of Medicine* [*New Engl. J. Med.*] **255**, 1179–1183, Dec. 20, 1956. 24 refs.

This paper on the incidence of primary cancer of the liver in relation to cirrhosis from the Mallory Institute of Pathology at the City Hospital, Boston, forms a natural sequel to the work on the same subject by F. B. Mallory himself, who in 1932 analysed the records of 9,346 necropsies performed at that hospital between 1897 and 1932 and noted amongst them 12 cases of primary cancer of the liver. The present author deals with the 23,114 necropsies performed from 1917 to 1954, thus including part of the period dealt with by Mallory. In this period of 37 years 108 cases of primary carcinoma of the liver were found. Among them, 82 cases (75·9%) were associated with cirrhosis, the incidence of carcinoma in all patients with hepatic cirrhosis being 3·4%, compared with Mallory's figure of 2·2%.

The question arises how the increased incidence has come about. Cirrhosis of the liver has increased in incidence in Boston from 8·5% of all necropsies in previous years to 13·93% in the period 1947–54. This increase has certainly not been in cases of cirrhosis associated with haemochromatosis, with syphilis, or with cardiac failure—all well known to Mallory—but seems chiefly to have been in cases of healed acute yellow atrophy (necrosis) of the liver resulting in cirrhosis, the cause of which has undoubtedly been the prevalence of acute viral hepatitis in recent years, while alcoholism, with poor dietary intake, has also increased.

The author, in considering the occurrence of primary carcinoma in these cases, rightly draws attention to the greater longevity of the population. He suggests that the question of the association of primary cancer of the liver with healed acute yellow atrophy requires further study.

[A good bibliography dealing with primary cancer of the liver (but not in tropical countries where the incidence is very different) is appended.] *J. W. McNee*

83. **Blood Pyruvic-acid and *alpha*-Ketoglutaric-acid Levels in Liver Disease and Hepatic Coma**

A. M. DAWSON, J. DE GROOTE, W. S. ROSENTHAL, and S. SHERLOCK. *Lancet* [*Lancet*] **1**, 392–396, Feb. 23, 1957. 5 figs., 21 refs.

The liver plays an important role in intermediate carbohydrate metabolism and the raised blood keto-acid levels reported in severe liver disease might be regarded as a sign of failure of this process. Paper chromatography makes it possible to analyse separately α-ketoglutaric and pyruvic acid which are transported from the periphery to the liver, and the blood levels of both these acids have been reported to be increased in hepatic coma.

An attempt was therefore made at the Postgraduate Medical School of London to determine the mechanism of the changes in blood keto-acid levels and to assess the clinical usefulness of their determination. For this purpose 38 patients with liver disease were studied, of whom 33 were suffering from portal cirrhosis, one from biliary cirrhosis, 2 from acute virus hepatitis, and one from Hodgkin's disease with jaundice and hepatic coma, while one had the typical neurological changes, a large extrahepatic portal–systemic collateral circulation, but a normal liver macroscopically and histologically. The neurological condition was assessed in 4 grades from 0 (normal) to 3 (coma). Removal of ammonium by the brain and peripheral tissues is reflected in an arteriovenous difference in blood ammonium content. This removal is probably due to the combination of α-ketoglutaric acid and ammonia to form glutamic acid, which by the addition of a second molecule of ammonia forms glutamine. It has been suggested that in hepatic coma the excess metabolized ammonium continues to combine with α-ketoglutaric acid in muscle and brain until the supply of this acid is exhausted, thus interfering with the working of the Krebs tricarboxylic acid cycle for which α-ketoglutaric acid is essential. The blood keto-acid levels were therefore compared with those of ammonium. In fasting patients with hepatic cirrhosis but without neurological signs the mean level of α-ketoglutaric acid in venous blood was raised, but that of pyruvic acid was normal. Both levels rose progressively as the neuropsychiatric state deteriorated to hepatic coma, but there was no correlation between the arterial level of ammonium and the venous level of α-ketoglutaric acid or pyruvic acid and in individual patients the values for each keto-acid were not sufficiently predictable to be of practical clinical value in diagnosis or management. There was

no constant pattern of change in blood α-ketoglutaric acid level when 10 cirrhotic patients were given 3 g. of ammonium chloride by mouth. Thioctic acid, a co-enzyme for the working of the tricarboxylic acid cycle and hence for the metabolism of pyruvic acid, was given to 4 patients in hepatic pre-coma without constant effect on the clinical state or blood keto-acid level.

E. Forrai

84. **Hepatic Insufficiency: a Report of Thirty-two Necropsied Cases**
M. FELDMAN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 264–267, March, 1957. 12 refs.

85. **Intrahepatic Cholestasis (" Cholangiolitis ")**
H. POPPER and P. B. SZANTO. *Gastroenterology* [*Gastroenterology*] **31**, 683–699, Dec., 1956. 6 figs., 32 refs.

The problem of complete or incomplete cessation of bile flow in the absence of extrahepatic biliary obstruction is not a new one, but its recent prominence dates from the work of Steigman and Popper published in 1943 (*Gastroenterology*, **1**, 645), while Watson and Hofbauer (*Ann. intern. Med.*, 1946, **25**, 195; *Abstracts of World Medicine*, 1947, **1**, 166) brought into use the term " cholangiolitis " [by which the condition is usually known].

The present authors state that although the condition (which they prefer to call " intrahepatic cholestasis ") is often caused by viral hepatitis, by exposure to certain drugs, or by primary biliary cirrhosis, in many cases the aetiology may be quite unknown. Moreover, the exact morphological changes in the liver and their sequence have remained a puzzle which the authors have attempted to solve by the study of clinical and biochemical data and biopsy and necropsy material from 31 cases of hepatitis and cirrhosis with and 31 without evidence of intrahepatic cholestasis, from 19 cases of intrahepatic cholestasis without known exposure to drugs, and from 30 cases of extrahepatic cholestasis. Photomicrographs [of excellent quality] illustrating the morphological changes at different stages in cases of intrahepatic cholestasis are provided, and comparisons are made with the histological picture in other forms of ultra-hepatic jaundice. They conclude from their personal observations that intrahepatic cholestasis is not regularly associated with any specific morphological changes except increased deposition of bile pigment, which is the result and not the cause of the condition. Inflammatory changes may be completely absent.

The authors then suggest a hypothesis based not only on their own studies, but also on those of others. They assume that the lesion starts with increased permeability of the ductules (or bile canaliculi), leading to biliary regurgitation. Inspissation of the bile at this stage adds an obstructive element. The bile which has leaked out from the canaliculi eventually excites inflammation around them and this inflammation is followed by fibrosis, thus adding a second obstructive element as the lesion progresses to its later stages. They finally state that in their opinion intrahepatic cholestasis [that is, cholangiolitis] can be unequivocally differentiated from extrahepatic biliary obstruction only in the rare cases in which the latter produces dilatation of the bile ducts, bile infarcts, and extravasation of bile into the portal tracts.

J. W. McNee

INTESTINES

86. **Functional Diarrhea: an Analysis of the Clinical and Roentgen Manifestations**
M. H. KALSER, D. E. ZION, and H. K. BOCKUS. *Gastroenterology* [*Gastroenterology*] **31**, 629–646, Dec., 1956. 7 figs., 12 refs.

The authors, from the University of Pennsylvania, report the results of an extensive investigation of functional diarrhoea. A total of 98 patients with gastrointestinal symptoms were divided into two groups—69 patients with diarrhoea and 29 control patients without diarrhoea. The presence of significant organic disease was considered to have been excluded in both groups. Emotional factors were held to be responsible for the diarrhoea in 45 of the patients, while the history in 7 suggested that the diarrhoea was the result of acute infection. It is emphasized that once the diarrhoea has started as the result of emotional trauma it may continue for months or years, with periods of equally troublesome constipation. Associated symptoms in a high proportion of cases were nausea and vomiting and abdominal pain of varying type, severity, and location; this pain was commonly felt in the lower abdomen before, and was relieved by, defaecation. Achlorhydria, although more frequently found in patients with diarrhoea than in those without, was not a common aetiological factor. On radiological examination there appeared to be a significant increase in patients with diarrhoea in the incidence of hypermotility of the small gut and of coarsening of the jejunal mucosa. Abnormalities of colonic function were not more marked in those with diarrhoea than in those without.

J. N. Harris-Jones

87. **Primary Nonspecific Ulcers of the Small Intestine: Clinicopathologic Study of 18 Cases with Follow-up of 14 Previously Reported Cases**
C. G. MORLOCK, H. R. GOEHRS, and M. B. DOCKERTY. *Gastroenterology* [*Gastroenterology*] **31**, 667–680, Dec., 1956. 6 figs., 4 refs.

A further study of the clinical and pathological features of primary nonspecific ulcers of the small intestine is reported from the Mayo Clinic, the authors analysing their findings in 18 new cases and the results of a follow-up investigation of 14 previous cases.

The commonest symptom, cramping mid-abdominal pain, was found to be related to obstruction of the small intestine. Haemorrhage from these ulcers was much less common, occurring only in a few instances. There were no localizing physical signs of any note. Because of the obstructive nature of the lesion radiological examination was possible only in 9 cases; in 3 of these no lesion of the small intestine was found, while in 6 the site of the obstruction was located, but no pathogno-

monic signs could be demonstrated. The ulcers did not give rise to generalized peritoneal soiling, but in some cases perforation with limited abscess formation was found at operation. Although patients who had other organic intestinal lesions, to which these ulcers may have been secondary, were excluded from the investigation, an accompanying duodenal ulcer was found in one case.

The pathological findings confirmed the non-specific nature of the ulcers, which in most cases showed a tendency to heal with fibrosis; the ulcers were usually solitary. Treatment consisted in surgical resection of the affected area, with entero-anastomosis. The mortality rate (11%) was considerably lower than that in other reported series. The authors state that the prognosis following successful operative treatment is good, there being little tendency to recurrence. *J. N. Harris-Jones*

88. **Problems in the Management of Ulcerative Colitis, with Particular Reference to ACTH and the Adrenal Steroids**

M. SKLAR, J. B. KIRSNER, and W. L. PALMER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 1–20, Jan., 1957. 6 figs., 21 refs.

The authors report, from the University of Chicago, their experience in treating 180 cases of ulcerative colitis with ACTH (corticotrophin), cortisone, and related compounds between 1950 and 1955. To this treatment 160 of these patients showed a satisfactory response and only 6 out of the 12 deaths in the series could be related in any way to hypercorticism. An analysis of comparable experience in the period before the introduction of these hormones showed that 55 out of 100 patients improved with medical treatment, and that of 14 who died, death in 9 cases was due to colonic perforation. Generally treatment consisted in 120 units of corticotrophin daily, but they found that prednisone was more useful in certain circumstances.

In discussing their experiences, which are illustrated by case histories, the authors stress that certain fears with regard to corticoid therapy have proved unfounded, namely, that the incidence of perforation, haemorrhage, or giant ulceration would be increased, that general infections would be masked, that the risk of peptic ulcer would be increased (only one of their 180 patients developed a peptic ulcer, and of 12 with a history of ulcer, all were given corticoid therapy without misadventure), and lastly that wound healing after surgery would be delayed. In their opinion the healing of wounds is related more to the patient's nutritional state, and the incidence of perforation and of haemorrhage to the severity of the disease. On the other hand the dangers of corticoid therapy provoking hypokalaemia, hypochloraemia, and psychotic disturbances are real and serious. The electrolyte disturbances must be treated energetically by intravenous infusions, at first of necessity, and later for preference, since potassium chloride by mouth has a laxative action. Later still, when the patient is well on the road to recovery, potassium by mouth may be tolerated. The authors note that psychotic disturbance is often ushered in by scalp paraesthesiae, paranoid ideas, restlessness, and excitement, and the appearance of these signs is in their view an indication for the withdrawal of corticoid therapy. The treatment may cause oedema and hypertension which may be troublesome, but these can be minimized by restriction of salt intake or the substitution of prednisone for corticotrophin. *J. Naish*

89. **The Natural History of Ulcerative Colitis**

E. R. CULLINAN and I. P. MACDOUGALL. *Lancet* [*Lancet*] **1**, 487–489, March 9, 1957. 3 refs.

The natural history of ulcerative colitis was studied in 346 cases treated at the Gordon Hospital, London, during an 8-year period ending June, 1955. The cases were divided into 3 groups: Group A, diffuse disease involving the whole of the colon; Group B, involvement of part of the colon continuous distally to the rectum; and Group C, sigmoidoscopic but not radiological evidence of ulcerative colitis. Cases of segmental colitis, which were few, were omitted from the series. At the time of the last examination 133 patients were in Group A, 145 in Group B, and 68 in Group C.

Only in a few cases could the course of the disease be predicted—namely, in 2 with fulminating disease, in 27 with unremitting severe symptoms, and 11 in which there were annual or biannual relapses with persistent regularity. In the remaining 306 cases the duration of remission and the severity of the relapses were unpredictable. In 70% of the cases the duration of the disease was more than 5 years and in about 2% it was more than 30 years. The mode and severity of onset bore little relation to the subsequent pattern of the illness.

The severity of the disease was related to the extent of colon involved. Thus in 57% of the patients in Group A and 18% in Group B the symptoms were "severe" or "very severe". About one-fifth of those in Group A, more than half of those in Group B, and almost three-quarters of Group C had trivial symptoms or no symptoms at all after treatment. Mortality in Group A was 5% and in Group B 5·3%; there were no deaths in Group C. Local complications did not influence mortality as much as systemic complications such as leucocytosis, anaemia, malnutrition, pyodermia, and thrombophlebitis. Carcinomata developed in 6 cases.

None of the patients had any previous history of colonic disorder. The onset was usually abrupt, and initially the disease was seldom severe. The authors do not discuss the aetiology of the condition, but note the importance of psychological factors. Of the 100 women in the series who had been pregnant, about one-quarter related the onset of the disease to pregnancy or the puerperium. The authors have had little success with chemotherapeutic agents. They state that only certain patients responded to cortisone and ACTH, usually those experiencing a severe attack, when the improvement was striking and often led to complete remission. Surgical treatment—that is, colectomy—should be carried out in all cases of the diffuse type of ulcerative colitis if there is no rapid improvement in response to conservative measures. *A. Gordon Beckett*

Cardiovascular System

90. **Effect of Pituitrin in Reducing Portal Pressure in the Human Being. Preliminary Report**
W. D. DAVIS, R. GORLIN, S. REICHMAN, and J. P. STORAASLI. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 108–111, Jan. 17, 1957. 3 figs., 6 refs.

It has been known for many years that posterior pituitary extract has a marked depressor effect on the pressure in the portal vein. In 2 patients with portal hypertension studied at the U.S. Naval Hospital, Portsmouth, Virginia, a very significant fall in portal pressure occurred when 20 units of vasopressin was injected intramuscularly. Portal pressures were measured by the splenic-puncture technique, and the falls of pressure induced were from 35 to 22, and from 22 to 14 mm. Hg respectively. Further studies showed that during these changes the cardiac output and liver oxygen consumption were unchanged, but the liver blood flow was reduced. This effect of posterior pituitary extract is suggested as potentially valuable in the treatment of bleeding oesophageal varices, though the authors have not yet had an opportunity to test the possibility. *J. McMichael*

91. **The Oesophageal Lead of the Electrocardiogram in Cardiac Insufficiency.** (Пищеводное отведение электрокардиограммы при пороках сердца)
V. I. MASLYUK. *Терапевтический Архив* [*Ter. Arkh.*] **29**, 50–63, No. 1, Jan., 1957. 9 figs., 16 refs.

Working at the 1st Moscow Medical Institute, the author has recorded standard, precordial (CF), and oesophageal electrocardiographic leads from 50 normal control subjects and 137 patients with cardiac insufficiency (83 with mitral lesions, 36 with combined mitral and aortic lesions, 16 with aortic lesions only, and 2 with patent ductus arteriosus). The electrode of the oesophageal lead was contained in a standard duodenal tube and was connected to the right arm lead, the usual left arm electrode being placed on the right arm. Oesophageal tracings were recorded from a standard position at the level of the border between left atrium and left ventricle and from two additional positions, one 3 cm. above and one 3 cm. below the standard level.

In patients with mitral lesions the oesophageal leads showed increase in the amplitude of the P wave with diminution in the amplitude of R and S waves. The extent of these changes was proportionate to the degree of decompensation. For purposes of comparison the author used the relation of the height of the P wave to the algebraic sum of heights of the R and S waves (P:QRS ratio). In normal controls this ratio was 0·2 to 0·3, but in patients with mitral lesions it was 1·3 to 2·0 or even 3·8. The higher the degree of circulatory insufficiency, the higher the P:QRS ratio.

In cases of combined mitral and aortic lesions the P:QRS ratio was also increased (usually 0·8 to 1·8), the voltage of the R and S waves being reduced, though the S wave was more marked than in cases with mitral disease alone. The author found that the height of the P wave was increased in the oesophageal leads even in cases of mitral stenosis in which it was normal in the standard and precordial leads.

In 12 of the 16 patients with aortic lesions the height of the S wave was markedly increased, and in the recording from the level of the atrio-ventricular junction it was 3 times greater than in the controls. S-wave changes in the oesophageal leads were more constant than left axis deviation in standard leads.

P-wave changes occurred in the oesophageal tracings in 95·7% of 96 cases of mitral or mitral and aortic disease, while such changes were seen in only 46·1% of standard and precordial recordings. Because of this and because the appearance of P-wave changes may precede the appearance of *x*-ray evidence of left atrial enlargement the author considers that the oesophageal leads are more useful in the diagnosis of cardiac disease than the standard or precordial leads.

Marcel Malden

CONGENITAL HEART DISEASE

92. **Patent Ductus Arteriosus in Infancy**
S. R. BAUERSFELD, P. C. ADKINS, and E. M. KENT. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **33**, 123–132, Jan., 1957. 1 fig., 12 refs.

During the past 3 years a diagnosis of patent ductus arteriosus was made and confirmed at operation or necropsy in 74 children of all ages at the Children's Hospital of Pittsburgh, 55 of the patients (74%) being females and 19 (26%) males. This paper deals primarily with the 22 infants (30%) who were under 2 years of age, since this group contained cases presenting both the most obvious and the least obvious symptoms of the anomaly.

Patent ductus arteriosus is usually asymptomatic in early infancy, but in some cases, of which this group was representative, there is poor weight gain, dyspnoea, frequent respiratory infections, and intermittent minimal cyanosis. The diagnosis is readily made clinically when the characteristic continuous murmur is present, but often only a systolic murmur is heard—as occurred in 12 of these 22 cases—usually in the pulmonary area, but in 3 cases the thrill and murmur were maximal along the left sternal border. In order to differentiate this condition from a high ventricular septal defect, retrograde aortography via the left carotid artery was employed. (This procedure was carried out on 43 infants during the 3 years, with 2 deaths.) Of the 22 infants here discussed, 2 died before operation could be performed, but closure was performed on the other 20, without an operative death. Two of the infants have since died, but follow-up

of the remaining 18 showed that they have all done well. The authors consider that if an infant has a shunt at two levels, for example, a patent ductus arteriosus and also a patent interventricular septum, then the two lesions exert an additive effect and benefit will result from closure of the patent ductus. *R. G. Rushworth*

93. **Patent Ductus Arteriosus with Reversal of Flow. Clinical Study of Ten Children**
R. C. ANDERSON, P. ADAMS, and R. L. VARCO. *Pediatrics* [*Pediatrics*] **18**, 410–423, Sept., 1956. 4 figs., 27 refs.

The clinical features in 10 cases of patent ductus arteriosus with reversal of flow are described in this paper from University Hospitals, Minneapolis, Minnesota. The patients, all children, had cyanosis, often greater in the toes, and dyspnoea on exertion had developed early in life. The electrocardiogram showed right ventricular hypertrophy in all cases. Cardiac catheterization indicated bidirectional shunt through the duct in 6 cases; in one case there was a reversed shunt flow only, while in 3 the data did not permit a definite conclusion to be reached.

Ligation of the patent ductus was successfully accomplished in one instance with significant clinical improvement. Examination of lung biopsy specimen in this case revealed only minimal pulmonary arterial changes. In 2 other cases ligation was followed by irreversible cardiac arrest, which occurred immediately after ligation in one case and 3 hours afterwards in the other.

The authors review 45 cases from the literature, the majority of which were in adults. In 22 of these surgery was performed, with good results in 4. In their view surgical treatment is likely to be disappointing in adults, but may be more successful when carried out early in life. *Gerald R. Graham*

94. **A Surgical-pathologic Classification for Isolated Ventricular Septal Defects and for Those in Fallot's Tetralogy Based on Observations Made on 120 Patients during Repair under Direct Vision**
H. E. WARDEN, R. A. DEWALL, M. COHEN, R. L. VARCO, and C. W. LILLEHEI. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **33**, 21–44, Jan., 1957. 11 figs., 19 refs.

Observations on 87 patients with isolated ventricular septal defect and 33 with Fallot's tetralogy who underwent surgical repair under direct vision with total cardiac by-pass at the University of Minnesota Hospitals, Minneapolis, showed that the anatomical classification of these defects by Rokitansky (which largely agrees with the embryological findings of Spitzer) provided an accurate working basis for the surgeon with only minor modifications, such as the addition of a traumatic type of septal defect, of which the authors had one case.

The most common septal defect encountered was that of the pars membranacea, and as the patients were selected for operation on the basis of severity of clinical symptoms it was considered that this type of lesion was particularly detrimental to the patient. More important than the size of the defect was its relation to the pulmonary artery—severe clinical disability was associated with even small defects if they were so situated that the jet of blood from the left ventricle was directed into the orifice of the pulmonary artery.

The methods of repair are briefly described. The authors believe that it is probably wise to correct a co-existing anomaly either before or coincidentally with the repair of the ventricular defect.

R. G. Rushworth

95. **Chest Pain in Patients with Isolated Pulmonic Stenosis**
R. P. LASSER and G. GENKINS. *Circulation* [*Circulation (N.Y.)*] **15**, 258–266, Feb., 1957. 4 figs., 34 refs.

At Mount Sinai Hospital, New York, the authors have observed 5 patients with congenital isolated pulmonary stenosis and typical angina pectoris or acute prolonged coronary insufficiency, but without frank evidence of myocardial necrosis. In all the patients the cardiac ischaemic pain was relieved by pulmonary valvotomy. In a discussion the authors state that the pain is due to right ventricular myocardial ischaemia, and that the factors which impair coronary circulation are: (1) very high right ventricular intracavitary systolic pressure and prolongation of right ventricular systole; (2) fixed low cardiac output; and (3) high right atrial and ventricular diastolic pressures which reduce the coronary arteriovenous pressure gradient. Further, the same factors could account for angina in pulmonary arterial hypertension due, for example, to mitral stenosis or chronic lung disease. The authors briefly mention 5 fatal cases of severe isolated pulmonary stenosis in which the necropsy findings revealed extensive patchy fibrosis of the right ventricle, the left ventricle being spared. *K. G. Lowe*

96. **Pulmonary Stenosis with Closed Ventricular Septum**
M. TORNER-SOLER, J. M. MORATÓ-PORTELL, and I. BALAGUER-VINTRÓ. *American Heart Journal* [*Amer. Heart J.*] **53**, 213–231, Feb., 1957. 14 figs., 24 refs.

In this report from the University of Barcelona the authors review 15 cases of pulmonary valvular stenosis with closed interventricular septum, of which 13 were verified by cardiac catheterization, and 7 also by angiocardiography, 6 at operation, and 2 at necropsy. Of the 7 male and 8 female patients, whose ages ranged from 2 to 44 years, 8 were cyanosed owing to a right-to-left shunt through a patent foramen ovale (4 cases), or to heart failure (3), or to entry of systemic veins into the left atrium (1 case), while 4 suffered from syncope, usually on effort, which was due to the obstruction to cardiac output caused by the valve lesion. All 15 had the characteristic murmur and thrill, and 13 had a pulmonary second sound that was soft or "practically inaudible".

Radiography revealed post-stenotic dilatation of the pulmonary artery in 14, increased pulsation of the pulmonary trunk in 14, and various degrees of cardiac enlargement. Electrocardiography showed right ventricular hypertrophy in all, P waves over 2 mm. tall in Lead II in 12 cases, atrial fibrillation in one, and right bundle-branch block in 3. On cardiac catheterization the pulmonary artery was entered in 7 cases, and an

abrupt rise in pressure was recorded on withdrawal of the tip of the catheter into the right ventricle, where systolic pressures up to 140 mm. Hg were recorded. The pressure curve in the ventricle was characteristic, being tall, domed, and symmetrical, and in some cases there was a temporary negative pressure in systole immediately above the pulmonary valve (the Venturi phenomenon).

The authors state that 5 of their 15 patients were of subnormal physique [criteria not given] and believe that this can best be correlated with the presence of cyanosis. The prognosis depends, of course, upon the severity of the lesion, and 2 of their female patients, aged 32 and 42 respectively, have little disability. They believe that surgery should be considered in all cases in which the right ventricular systolic pressure is over 100 mm. Hg, or where electrocardiography shows severe right ventricular hypertrophy, with ST–T depressions in leads V1 to V4 or beyond. In 6 of the authors' cases transventricular direct pulmonary valvotomy of the Brock type was performed [but the surgical results are not discussed; one of the 6 patients died]. *J. A. Cosh*

CHRONIC VALVULAR DISEASE

97. **Syphilitic Aortic Incompetence with Special Reference to Prognosis and Effect of Treatment**
J. C. LEONARD and W. G. SMITH. *Lancet* [*Lancet*] **1**, 234–240, Feb. 2, 1957. 4 figs., 34 refs.

Most previous studies of the prognosis in syphilitic aortic disease have emanated from the United States and have included a considerable number of negro patients. The study here described was undertaken in an attempt to determine the prognosis of syphilitic aortic incompetence as seen in Great Britain and to assess the value of different forms of treatment, including that with penicillin. The series consisted of 374 cases of aortic incompetence with no other valvular lesion diagnosed during the period 1926–55, of which 276 were seen at the London Hospital (93 cases) and the National Heart Hospital, London (183). In 360 cases the Wassermann or Kahn reaction was positive, while in the rest there was other evidence of syphilis. About two-thirds of the patients (269) were males, 2 were negroes, one Chinese, and the rest were of European origin; the mean age was 54 and the maximum incidence (134 cases) was in the sixth decade of life.

In 111 of the cases (30%) there was a history of primary syphilis or gonorrhoea, and the mean interval from primary infection to diagnosis of aortic incompetence was 31 years (range 8 to 52 years). The commonest symptoms were dyspnoea on exertion and cardiac pain. In 18 cases there was marked loss of weight and in these the prognosis was worse. Systolic thrills were observed in 42 patients who had no evidence of aneurysm, an Austin Flint murmur was noted in 29, and auricular fibrillation in 26. The erythrocyte sedimentation rate was raised in many cases, especially if no treatment had been given, but effective treatment lowered the rate slowly over many months. Calcification of the ascending aorta was noted in 22 (35%) of 64 cases in which the radiographs were personally examined. Expected abnormalities in the electrocardiogram were seen in the majority of cases. At the time of the report 222 of the patients were dead, 102 alive, and 50 (13%) could not be traced. The mean survival time after diagnosis among those who had died was 48 months. Calculation of the percentage survival by the life-table method showed that 75% survived for 1 year, 54% for 5 years, 32% for 10 years, and 14% for 20 years after diagnosis, females having a better prognosis than males after the first year. In 49 cases there were no symptoms at the time of diagnosis and of these patients 42 (85%) were alive at 5 years. Of 180 patients with cardiac pain, 121 died after a mean survival time of 73 months from the time of onset of angina. Heart failure was present in 111 cases, and the mean survival of the 89 such patients who died was only 18 months. The impression that patients with a low diastolic blood pressure have a poorer prognosis was confirmed. The prognosis was found to grow steadily worse with increasing age, heart failure being more frequent in older patients. As stated, the prognosis was better in females, the mean survival time for all men being 42 months, whereas for all women it was 66 months. [On the whole the women were younger than the men and the authors have not separated the effects of sex, age, and heart failure on survival.]

Full details are given of previous treatment and its relation to survival time [but the various groups are small and little statistical correlation is attempted]. After 10 years 60% of a fully treated group (total 28) survived, in contrast to 31% of an inadequately treated group (27 patients), this difference being significant. The authors found no evidence of a prognostic difference between patients adequately treated with either arsenic or bismuth alone and those treated with penicillin in addition. Patients treated with penicillin alone seemed to fare slightly worse. The authors issue the caution that their conclusions are to be regarded as provisional.
David Friedberg

CORONARY DISEASE AND MYOCARDIAL INFARCTION

98. **The C-Reactive Protein Determination as an Index of Myocardial Necrosis in Coronary Artery Disease**
I. G. KROOP and N. H. SHACKMAN. *American Journal of Medicine* [*Amer. J. Med.*] **22**, 90–98, Jan., 1957. 10 figs., 20 refs.

Serial tests for the presence in the serum of C-reactive protein were carried out on 100 patients with coronary arterial disease; from the results, which are described in this paper from the Jewish Chronic Disease Hospital and the State University of New York, Brooklyn, the authors conclude that the presence of this factor is a sensitive index of myocardial necrosis or inflammation, provided there is no inflammation of infectious or non-infectious origin elsewhere in the body. In 34 patients with transmural myocardial infarction and an electrocardiogram (ECG) showing Q waves and progressive changes in RS–T and T waves, the response to the C-

reactive protein test was positive within 12 to 72 hours after the onset of pain; it reverted to negative in the 2nd to 5th weeks, although the erythrocyte sedimentation rate might still be increased. Reappearance of C-reactive protein in the serum of such patients denoted recurrence of myocardial infarction or complications such as phlebothrombosis or gout. In 5 patients in the premonitory phase of transmural infarction (with angina or acute coronary insufficiency and ECG changes only in the RS–T and T waves) the response to the test was negative, but became positive as frank transmural infarction developed. In 6 patients with old transmural infarction and persistent Q waves who experienced a recurrence of ischaemic heart pain a positive result in the C-reactive protein test indicated further myocardial necrosis. Of 55 patients without Q waves in the ECG but with either angina or acute coronary insufficiency, the response to the test was negative in 35 and positive in 20, a positive result being accepted as indicating the presence of myocardial necrosis. *K. G. Lowe*

99. **Medical Evaluation of the Beck Operation for Coronary Artery Disease**

B. L. Brofman. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **162**, 1603–1606, Dec. 29, 1956. 5 refs.

The author has evaluated the results of the operation described by Beck and Leighninger (*J. Amer. med. Ass.*, 1955, **159**, 1264; *Abstracts of World Medicine*, 1956, **19**, 462), which consists essentially in "mechanical abrasion of the epicardium and parietal pericardium, partial ligation of the coronary sinus, instillation of powdered asbestos, and the application of mediastinal fat and pericardium to the heart", the object being to stimulate intercoronary arterial communication and improve the blood supply to the myocardium.

At the University and Mount Sinai Hospitals, Cleveland, Ohio, 185 patients have been thus operated upon since January, 1951, with 11 deaths associated with surgery, a mortality rate of 6%. Such patients are divided into three groups: (1) those with mild symptoms, who may have had a small infarct or mild angina; (2) those with hearts of normal size and moderate to severe angina who may have had one or more infarcts; (3) those who have suffered severe myocardial damage and who may have a large heart or congestive heart failure; patients with status anginosus fall into this group. The majority of patients operated on so far belonged to Group 2, but the number of those in Group 1 is increasing.

A recent myocardial infarction precludes operation for 4 to 6 months. Cardiac enlargement and congestive failure are relative contraindications to operation, as also is severe hypertension. Operation is hazardous in younger patients with rapidly progressive symptoms. Three-quarters of the patients operated on had had a myocardial infarct and 95% had angina pectoris of variable severity. Long-term follow-up studies carried out on 137 consecutive patients operated on 6 months to 5 years previously showed that 18 (13·1%) are known or presumed to be dead (compared with an expected mortality of 30% in untreated patients), that 90% of the survivors have had a complete or considerable reduction of anginal pain, and that 90% are able to work normally or with slight restrictions, compared with only 45% before operation. *W. P. Cleland*

100. **Effect of Cigarette Smoking on Coronary Blood Flow and Myocardial Metabolism**

L. M. Bargeron, D. Ehmke, F. Gonlubol, A. Castellanos, A. Siegel, and R. J. Bing. *Circulation* [*Circulation (N.Y.)*] **15**, 251–257, Feb., 1957. 2 figs., 29 refs.

The authors of this paper from the Medical College of Alabama, Birmingham, Alabama, describe an investigation into the effect of cigarette smoking on the coronary blood flow and myocardial metabolism in 30 adult volunteers without evidence of coronary disease. In 14 of the 30 subjects coronary-sinus catheterization was successfully performed and in 12 of these the coronary blood flow was determined by the nitrous oxide method before and during the smoking of a cigarette. In 11 of these subjects the coronary blood flow rose significantly from a mean of 69·8 ml. to a mean of 82·8 ml. per minute per 100 g. of heart muscle. There was an associated significant fall in coronary vascular resistance. The myocardial extractions of oxygen and glucose declined with the rise in coronary blood flow, but myocardial usage of both oxygen and glucose was unchanged. There was a fall in myocardial extraction of pyruvate and a rise in that of ketones, but the changes were not statistically significant. None of the subjects had heart disease. The published findings of others on the effects of nicotine on coronary blood flow in the atherosclerotic rabbit and the effects of smoking on the electrocardiogram and ballistocardiogram of patients with coronary arterial disease suggest, however, that nicotine reduces coronary blood flow in the presence of coronary arterial disease. *K. G. Lowe*

101. **Prognosis of Illness and Appearance of Q Waves on Electrocardiograms in Myocardial Infarction.** [In English]

V. M. Anttonen and A. Kasanen. *Annales medicinae internae Fenniae* [*Ann. Med. intern. Fenn.*] **45**, 175–182, 1956. 9 refs.

An analysis has been made of the electrocardiograms (ECGs) of 200 patients with myocardial infarction treated at the Medical Clinic of the University of Turku in Finland in an attempt to determine the prognostic significance of the development of prominent Q waves. In the ECG of 47 out of the 50 patients who died within 2 weeks of admission to hospital there was an early appearance of Q waves wider (over 0·03 sec. from onset to nadir) or deeper than normal, and in 62% both changes were present. In the ECG of 113 of the 150 patients who survived the first 2 weeks the early appearance of Q waves was also noted, and during the following weeks further Q-wave changes frequently appeared. However, the changes were not so marked in the survivors, for instance, in only 38% were the waves both wide and deep. It is thus concluded that the appearance of prominent Q waves during the first 3 days after a

myocardial infarction is of bad prognostic significance, whereas the later development of such Q waves is of little significance. *C. Bruce Perry*

102. **Management of Shock with Corticotropine (ACTH) in Myocardial Infarction.** [In English]
V. M. ANTTONEN and A. RAUTAKOSKI. *Annales medicinae internae Fenniae* [*Ann. Med. intern. Fenn.*] **45**, 183–194, 1956. 30 refs.

In an attempt to treat the shock associated with myocardial infarction ACTH (corticotrophin) was administered in 86 cases at the Municipal Hospital, Kuopio, Finland. The results were compared with those in 73 untreated cases. ACTH was given in doses of 10 to 350 units a day, the majority of patients receiving 40 to 160 units, and was usually given in the long-acting form. Of the treated cases, 60 exhibited clinical symptoms of shock, and of these, 14 died; of the 26 without symptoms of shock, 3 died. In the control series 19 patients exhibited shock, of whom 11 died, as did 7 of the 54 with no shock. No patient with profound shock survived. The treatment thus appeared to affect favourably the course of the disease in the moderately shocked patient. There was no evidence that the incidence of cardiac failure or of thrombo-embolic complications was increased by the treatment.

[The number of patients studied in each group is so small that the figures must be regarded as of doubtful significance.] *C. Bruce Perry*

HEART FAILURE

103. **Water Excretion in Cardiac Decompensation and Chronic Disease**
E. M. LASCHÉ and T. M. DURANT. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 80–86, Jan., 1957. 5 figs., 14 refs.

Employing the modification of the Kepler water-excretion test described by Oleesky (*Lancet*, 1953, **1**, 769; *Abstracts of World Medicine*, 1953, **14**, 497) the authors, working at Temple University School of Medicine, Philadelphia, have compared water excretion in 25 patients with intermittent or continuous cardiac decompensation which had been present for periods varying from 6 weeks to 14 years, and most of whom were decompensated at the time of study, in 14 patients who had been suffering from other chronic diseases such as diabetes mellitus or hepatic or renal disease for periods of one month to 20 years, in a series of normal control subjects, and also in 2 normal women to determine possible variations occurring during the menstrual cycle. For the test 700 to 1,200 ml. of water was administered over a period of 20 minutes, urine being collected every 20 minutes for 2½ hours. In most cases the test was repeated the following day, 75 mg. of cortisone being given orally 4 hours before the water. The maximum rate of urinary excretion per minute, the shape of the excretion curve, and the percentage of water load excreted in the 2½ hours by members of each group were compared.

The control subjects showed a maximum rate of urinary flow of 10·6 to 18 ml. per minute, which was achieved between 55 and 90 minutes after drinking the water, and they excreted from 50 to 170% of the load. Though the maximum rate of excretion for individuals varied, the form of the excretion curve remained similar. No definite pattern of variation occurred in the 2 women during the menstrual cycle, nor was there any significant change in water excretion after the administration of cortisone.

The patients with heart failure fell into two groups: (1) those (14 cases) in whom the maximum rate of excretion ranged from 2·4 to 8·7 ml. per minute and (2) those who failed to excrete more than 0·7 ml. per minute; patients with more recent onset of the cardiac condition and predominantly left-sided heart failure tended to belong more often to the less severely affected group. Maximum excretion generally occurred later after the ingestion of water (70 to 150 minutes) and the proportion of the load excreted in 2½ hours was also lower (11 to 64%) than in the controls in most instances. Of 12 patients in whom the test was repeated after the administration of cortisone, 7 showed a significant increase in the amount of water excreted (up to 150%), while of the remaining 5, only one showed a marked decrease in the percentage excreted. In the Group-2 cardiac patients the excretion curve was flat and cortisone produced no significant change. Of the 14 patients with other chronic conditions, although the maximum rate of excretion obtained was low, it was above 1 ml. per minute in all but one case. A significant increase in the percentage of the water load excreted occurred in only 3 of the 12 on whom the test was repeated after cortisone administration.

Water excretion is often as greatly impaired in heart failure as in Addison's disease. Similar but less severe impairment occurs in patients suffering from chronic diseases not associated with obvious water retention, but the administration of 75 mg. of cortisone did not produce as marked or as constant an effect in correcting this deficiency in either of these groups as has been reported in cases of adrenocortical insufficiency. The authors suggest that a state of functional adrenocortical insufficiency may exist in some cases of cardiac failure. The improved water excretion following administration of cortisone suggests that disturbance of the antidiuretic-hormone:adrenocortical-hormone ratio exists in them and that this ratio is favourably influenced toward the inhibition of secretion of the former by the administration of the adrenal steroid. *L. G. Fallows*

104. **Hydrothorax in Congestive Heart Failure**
G. A. RACE, C. H. SCHEIFLEY, and J. E. EDWARDS. *American Journal of Medicine* [*Amer. J. Med.*] **22**, 83–89, Jan., 1957. Bibliography.

At the Mayo Clinic between 1948 and 1953 necropsy was performed in 402 cases in which congestive heart failure was "a major or minor aspect" of the terminal illness, and the records of these were studied for the occurrence of hydrothorax. Altogether 112 cases were discarded because there was unilateral obliteration of a

pleural space or the amount of fluid present was less than 250 ml., the minimum adopted for a diagnosis of hydrothorax. In 255 (87·9%) of the 290 cases studied hydrothorax was bilateral; of the remainder, it was right-sided in 24 (8·3%) and left-sided in 11 (3·8%). Expressed in another way, 279 patients had fluid in the right pleural space and 266 patients had fluid in the left pleural space; thus the predominance of right over left hydrothorax was not impressive. There was no significant correlation between the side of the pleural effusion and such factors as pulmonary infarction, pneumonia, atrial fibrillation, and type of heart disease. Pulmonary oedema was present in 151 of the 255 patients with bilateral hydrothorax, in all 11 of those with unilateral left hydrothorax, and in 9 of the 24 patients with unilateral right hydrothorax; it was present in 177 (61%) of the total of 290 patients.

The authors were " unable to identify any one predominating factor as the cause of pleural effusion on the basis of congestive heart failure ". *K. G. Lowe*

BLOOD VESSELS

105. Necrotizing Panarteritis: a Complication of Repair of Coarctation of the Aorta

J. B. GROW, C. V. DEMONG, and W. R. RUNDLES. *American Surgeon* [*Amer. Surg.*] **22**, 1168–1173, Dec., 1956. 3 figs., 18 refs.

The authors point out that, although surgical repair of coarctation of the aorta is usually satisfactory, abdominal symptoms due to necrotizing panarteritis occasionally follow operation for coarctation, and in some cases have led to a fatal outcome. At post-mortem examination severe vascular changes are found, but occurring only below the level of the aortic suture. The muscular arteries of the mesentery show acute necrosis and inflammation, with destruction of the media. It is suggested that these changes may be due to the sudden increase in blood pressure and blood flow in vessels not supported by surrounding muscles which results from the operation.

One such case is described in detail; it occurred in an 8-year-old boy who developed abdominal pain and distension, with fever and leucocytosis, on the 5th day after excision of a coarctation, without other symptoms. On the 19th day laparotomy was performed and revealed hundreds of small gangrenous areas and minute perforations throughout the whole length of the small intestine, which was resected from the ligament of Treitz to near the caecum. After a stormy postoperative course during which there was violent diarrhoea and progressive loss of weight the patient died on the 69th day. Similar abdominal symptoms occurred in 6 other patients (out of a total of 72 operated on) but all recovered, in most cases within 7 to 10 days. In 2 cases treatment consisted in intestinal decompression, intravenous alimentation, and administration of antibiotics to sterilize the bowel—a regimen which the authors recommend if abdominal pain with fever follows operation for repair of coarctation of the aorta. *M. Meredith Brown*

106. Massive Thrombophlebitis

B. N. CATCHPOLE. *Lancet* [*Lancet*] **1**, 343–348, Feb. 16, 1957. 6 figs., 20 refs.

The author reports from the University of Sheffield 5 cases in which massive thrombophlebitis of the lower limb supervened on a pre-existing morbid condition and discusses the physiopathology, differential diagnosis, and treatment of this complication. The patients, 4 women and one man, ranging in age from 20 to 67, were suffering respectively from (1) carcinoma of the pelvic colon, for which colostomy had been performed, and classic " white leg " on one side; (2) puerperal oedema of both legs; (3) ulcerative colitis in early pregnancy with recurrent thrombosis in both legs; (4) carcinoma of the ovary with pelvic metastases; and (5) carcinoma of the pelvic colon with secondary deposits in the liver and lungs.

The accident is regarded as an extensive form of phlegmasia alba dolens, the oedema being caused by venous occlusion—the arteries remaining patent—augmented by capillary filtration as a result of the greatly increased pressure in the capillaries. In 2 cases onset was sudden, causing shock and circulatory failure from which one of these patients died. In the other 3 cases the signs, although severe, developed less rapidly, several attacks of phlebitis occurring successively so that the circulation was not suddenly depleted; nevertheless gangrene of the toes developed in every case. Massive thrombophlebitis can be distinguished from arterial occlusion by the unexpected occurrence of severe pain in the thigh, or less often near the knee, and the rapid development of gross oedema of the whole limb, extending up to the inguinal ligament or above, which is dusky purple in colour and persists on elevation of the limb; there may be petechial haemorrhages or blebs and the intense pain usually limits movement; peripheral pulses are present initially, and there is rapid refilling of subpapillary veins after pressure. Hyperaesthesia, paraesthesiae, and hypoaesthesia may occur in both acute venous and arterial occlusion.

The 2 cases of sudden onset in the series were treated by immediate transfusion of blood and glucose-saline, and in the surviving patient by elevation of the limb and passive movements for 12 hours, with good effect. In the other 3 cases transfusion was not required; no good result followed from the initial use of anticoagulants (in all cases), paravertebral block (one case), or administration of a vasodilator drug (one case), and it is considered that all these measures are contraindicated. Treatment was directed to aiding resolution by elevating the limb and encouraging early mobilization by physiotherapy. The optimum environmental temperature for a limb with incipient gangrene is about 68 to 77° F. (20 to 25° C.), which helps to reduce oxygen demand, and demarcation should be awaited in gangrenous tissue. With this treatment 2 of the surviving 4 patients recovered and the other 2 were improved, but died later from the original disease. Extensive venous occlusion was verified post mortem in 2 instances, the inferior vena cava being involved in both. The importance of correct diagnosis and immediate treatment is emphasized. *V. Reade*

HYPERTENSION

107. **Renal Haemodynamic Effects of Hypotensive Drugs. I. Acute Effects of Hexamethonium Bromide before and after Treatment with Reserpine**
B. GOLDBERG. *Lancet* [*Lancet*] **1**, 74–76, Jan. 12, 1957. 2 figs., 8 refs.

Hexamethonium was given intravenously to 13 hypertensive patients at the Middlesex Hospital, London, in doses sufficient to reduce the blood pressure with the patient in the recumbent position. During the fall of pressure the renal plasma flow fell, as also did urine flow and potassium and sodium excretion. Little significant alteration in these patterns of response took place when, in 5 cases, the hexamethonium was given during treatment with reserpine. At the height of the hypotensive effect of methonium salts there is usually renal vasoconstriction. This may be a consequence of vasodilatation and pooling of blood in the limbs leading to decreased cardiac output and diversion of blood from the kidneys. *J. McMichael*

108. **Renal Haemodynamic Effects of Hypotensive Drugs. II. Effects of Oral Maintenance Therapy with Pentapyrrolidinium Bitartrate and Reserpine**
L. MCDONALD and B. GOLDBERG. *Lancet* [*Lancet*] **1**, 77–78, Jan. 12, 1957. 9 refs.

The long-term effects of the oral treatment of hypertension with pentolinium and reserpine were observed at the Middlesex and National Heart Hospitals, London, in 6 patients, all but one of whom showed a satisfactory response of the blood pressure to the treatment. A slight lowering of the renal vascular resistance was observed, but the cardiac output and general renal haemodynamic patterns were little changed. *J. McMichael*

109. **A Comparison of the Effects of Phenobarbitone and Reserpine in Hypertension**
E. H. COOPER and W. I. CRANSTON. *Lancet* [*Lancet*] **1**, 396–397, Feb. 23, 1957. 4 refs.

In an attempt to determine the extent to which the hypotensive action of reserpine is due to its known sedative effect, a controlled trial was carried out on 11 patients with essential hypertension. Of these, 7 were observed during three 12-week periods in which they received, respectively, 0·5 mg. of reserpine 3 times a day, ¼ gr. (32 mg.) of phenobarbitone 3 times a day, and control tablets; the remaining 4 patients were observed during two similar periods in which they were given control tablets and reserpine respectively. Only the readings taken during the second 6 weeks of each observation period were analysed; the blood pressure in all patients had by that time become stabilized.

In all the patients there was a highly significant fall in blood pressure during the period of reserpine therapy, while in only three was there a fall in blood pressure during the period of administration of phenobarbitone. In the group as a whole (7 patients) phenobarbitone did not cause a significant fall in blood pressure.

[The results confirm what is now generally accepted from clinical experience, but this investigation is open to criticism on several grounds. In view of the small number of patients administration of phenobarbitone to less than two-thirds of them is hard to justify; the authors' assumption that the sedative effect of ½ gr. of phenobarbitone is equivalent to that of 0·5 mg. of reserpine seems to be unsound; the dosage of reserpine appears higher than is, in fact, found necessary in many cases of essential hypertension; and the need to determine the correct dose of reserpine for patients individually appears to the abstracter to make this type of investigation pointless.] *H. F. Reichenfeld*

110. **Treatment of Severe Arterial Hypertension: Results from Long-term Use of Methonium Compounds with and without the Addition of Reserpine**
A. J. BARNETT. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **5**, 274–290, Nov., 1956. 6 figs., bibliography.

At the Alfred Hospital, Melbourne, 67 patients with diastolic hypertension either in the malignant phase (32 cases) or with severe symptoms such as incapacitating headache or left ventricular failure were treated for periods of not less than 6 months. During the first phase of the 5-year study only methonium compounds given orally were used, in doses of about 1 g. three times a day; later parenteral hexamethonium (15 to 250 mg., average 100 mg., 3 times a day) and pentolinium (10 to 400 mg., average 100 mg., by mouth or 2·5 to 50 mg., average 15 mg., parenterally 3 times a day) were used, with reserpine (0·125 to 0·75 mg. by mouth 3 times a day) replacing the methonium in some cases.

Except for oral penta- and hexa-methonium, which produced only temporary reduction, continued control of blood pressure was usually possible with one or more of these agents. The combination of pentolinium with reserpine proved most satisfactory for long-term administration and yielded blood-pressure control which was classified as "good" (diastolic pressure <110 mm. Hg in the lying position) or "fair" (diastolic pressure between 110 and 120 mm. Hg) in almost all instances in which it was used. Relief of symptoms was striking and lasting, especially in respect of headache, effort dyspnoea, paroxysmal dyspnoea, and minor cerebral disturbances such as dizziness and black-outs. Angina pectoris improved in 5 out of 6 cases in which it was present, and only one patient developed anginal pain in association with drug-induced hypotension. There was objective evidence of improvement in the form of regression of ocular and cerebral signs, and papilloedema disappeared in almost all those who survived the malignant phase. Cardiac status tended to improve during the first year of therapy, and thereafter to remain stationary. There was no obvious improvement in renal function. Of the 32 patients with malignant hypertension, 23 survived for more than one year after beginning treatment and 12 (40%) for more than 2 years.

Altogether 21 patients, 14 of whom had malignant hypertension, died while under observation. The commonest cause of death was cerebral vascular accident (9 cases, in 4 of which necropsy was performed and revealed cerebral haemorrhage); this complication was

more likely to occur when the blood pressure was high than when it was low and its incidence did not appear to be increased by therapy. In 6 instances death was associated with renal failure, but again there was no evidence that treatment was a contributory factor. (Patients who were in uraemia when first seen were excluded from the trial and hypotensive drugs were used cautiously if renal function was shown to be markedly impaired, only moderate blood-pressure reduction being attempted.)

It is concluded that the methonium compounds are best given by injection and that pentolinium, especially in combination with reserpine, provides the most effective means of treatment in severe arterial hypertension. These drugs can produce continued blood-pressure reduction, considerable symptomatic relief, and regression of certain physical signs, and they appear to prolong significantly the life expectancy of patients with malignant hypertension. *S. G. Owen*

111. **Pressor Effects of Norepinephrine after Drastic Reduction of Sodium Intake**
L. K. DAHL. *Circulation* [*Circulation* (*N.Y.*)] **15**, 231–236, Feb., 1957. 6 refs.

In an investigation reported from Brookhaven National Laboratory, Upton, N.Y., the pressor response to intravenous infusion of noradrenaline before and after reduction in the dietary intake of sodium was studied in 8 hypertensive patients and in one patient with rheumatoid arthritis who served as a control. The low-sodium diet given provided 115 mg. of sodium daily. The dosage of noradrenaline was approximately the same in the individual patient in both dietary periods, but varied from patient to patient according to sensitivity to the drug. There was no uniform decrease in pressor response to noradrenaline during sodium deprivation as described by Raab *et al.* (*Circulation*, 1952, **6**, 373), and while the author discusses certain differences between the two studies which might explain the discrepancy, he concludes that " drastic limitation of sodium itself may be, but commonly is not, followed by a decreased pressor response to noradrenaline ". *K. G. Lowe*

112. **Use of Mecamylamine in the Management of Hypertension**
F. H. SMIRK and E. G. MCQUEEN. *British Medical Journal* [*Brit. med. J.*] **1**, 422–425, Feb. 23, 1957. 2 figs., 11 refs.

The efficacy of mecamylamine (" inversine "), a secondary amine, in the management over a period of 4 to 8 months of 40 patients suffering from hypertension is discussed in this paper from the University of Otago Medical School, Dunedin, New Zealand. Unlike the quaternary ammonium compounds pentolinium (" ansolysen ") and chlorisondamine (" ecolid "), which are tertiary amines, mecamylamine is almost completely absorbed from the alimentary tract, so that the effective oral dose is little higher than the parenteral dose. Since the effect of mecamylamine lasts for over 12 hours, the drug was given in the present series of cases twice or occasionally 3 times a day. The average daily dose for satisfactory control of hypertension was 33 mg.; in no case did it exceed 70 mg. Tolerance of the drug occurred occasionally, but was very minor in degree. However, mecamylamine was more often associated with parasympathetic side-effects than either pentolinium or chlorisondamine, these side-effects causing considerable discomfort in 25 of the 40 patients. Constipation and abdominal distension were reported in 14 cases, dryness of the mouth in 11, nausea and vomiting in 9, and dysuria and blurring of vision in 5 each.

The authors point out that other secondary amines as yet untested may prove to be more satisfactory as ganglion-blocking agents than any of those which are at present available. *A. G. Freeman*

113. **Evidence for an Increased Intake of Sodium in Hypertension Based on Urinary Excretion of Sodium**
L. K. DAHL. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **94**, 23–26, Jan., 1957. 11 refs.

From the year 1953 onwards all members of the staff of the Brookhaven National Laboratory, Upton, New York, were questioned (on the occasion of the annual medical examination) about their daily salt intake. In this rough and ready way the 1,346 adults concerned were divided into three categories, namely, those with: (1) a low-salt intake, consisting of 135 persons who did not add salt to their food at table; (2) an average intake, 630 who added salt if, after tasting, their food was insufficiently salty; and (3) a high intake, 581 who invariably added salt to their food before tasting. Analysis of the results showed that the 105 hypertensive subjects in the series were distributed as follows: low intake, 1, average intake, 43, and high intake, 61. Further, the low-intake group contained significantly fewer and the high-intake group significantly more cases of hypertension than would be expected by chance.

In previous studies the urinary sodium excretion had been shown to be a highly reliable measure of sodium intake, so 28 male subjects were selected from the series (on the basis of ease of co-operation and of getting adequate representation of hypertension in the three different intake groups) from whom 24-hour collections of urine were made for an average period of 9 days and the sodium output measured. Most of the subjects were unaware of the purpose of the study, and they did not vary their normal use of table salt during the investigation. The mean urinary sodium excretion for the 8, 9, and 11 members of the three intake groups, respectively, were 156, 169, and 202 mEq. per day. In these subjects hypertension was defined as a blood pressure of at least 140 mm. Hg systolic in combination with a diastolic pressure of at least 90 mm. Hg. By these criteria 9 out of the 28 had hypertension and these 9 had a significantly greater ($P<.01$) sodium intake (as indicated by urinary output) than did the non-hypertensive subjects.

These findings lend support to the hypothesis that the level of sodium intake is of primary aetiological importance in the development of essential hypertension. *P. Hugh-Jones*

Haematology

114. **Treatment of Polycythaemia Vera with Radioactive Phosphorus.** (Лечение больных истинной полицитемией радиоактивным фосфором)
M. I. Gol'dshteĭn and L. G. Prokhorova. *Советская Медицина* [*Sovetsk. Med.*] 25–28, No. 12, Dec., 1956.

The authors present their observations on 7 cases of polycythaemia vera treated since June, 1953, with radioactive phosphorus given in a dosage of 1 to 2 mc. at intervals of 6 to 8 days to a total of 6 to 8 mc. There were no undesirable reactions. Subjective improvement was observed during treatment, and objective improvement, which became manifest after 2 to 3 months, is stated to have been maintained. *R. Crawford*

ANAEMIA

115. **Clinical Diagnosis of Sickle-C Disease**
W. F. Denny, T. O. Finn, and R. M. Bird. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **99**, 214–217, Feb., 1957. 9 refs.

The heterozygous combination of haemoglobins S and C in the same person gives rise not to the benign sickle-cell trait, but to a haemolytic disease which can be differentiated clinically from the homozygous state associated with sickle-cell anaemia, and 5 cases of this " sickle–C disease " seen at the University of Oklahoma Hospitals, Oklahoma City, are here described. Their clinical features and those of 41 previously reported cases of sickle–C disease are contrasted with the findings in 16 cases of sickle-cell anaemia in which the diagnosis was confirmed by electrophoretic study of the haemoglobins. It is concluded that a clinical diagnosis of sickle–C disease can be made in a negro patient with arthralgia, abdominal pains, and splenomegaly whose blood gives positive sickle-cell preparations, yet contains more than 30% of target cells. In contrast, in pure sickle-cell anaemia the spleen is small and target cells few. It is pointed out that many of the cases of sickle-cell anaemia reported before the introduction of electrophoresis of haemoglobins were probably in fact cases of sickle–C disease. *A. G. Baikie*

116. **Erythrokinetics in Cooley's Anemia**
P. Sturgeon and C. A. Finch. *Blood* [*Blood*] **12**, 64–73, Jan., 1957. 2 figs., 33 refs.

The authors report the results of a study of blood production and destruction in 4 cases of Cooley's anaemia, 2 mild and 2 severe, in children aged 4½ to 13 at the Children's Hospital, Los Angeles. An increased turnover of haemoglobin constituents comparable to the maximum occurring in other haemolytic anaemias was found, but there was a marked decrease in the maximum delivery of erythrocytes to the peripheral blood, amounting to 50% in the mildly anaemic and to 85% in the severely anaemic patients. The rate of destruction of circulating erythrocytes, determined by the Ashby technique using radioactive chromium, was similar in the 3 patients studied, being 7 to 10 times the normal, but as the authors point out, this rate of destruction may be erroneously high either as a result of excessive elution or of damage to the erythrocytes by the chromium ion.

It is concluded that the defect in Cooley's anaemia is not in haemoglobin synthesis but in the fabrication of circulating erythrocytes, which in turn have the associated manifestations of hypochromia, increased percentage of foetal haemoglobin, and shortened survival time.
A. Ackroyd

117. **Iron Absorption Curves in the Treatment of Anaemias with Oral Iron**
A. J. Erenstrom. *New Zealand Medical Journal* [*N.Z. med. J.*] **55**, 462–471, Dec., 1956. 1 fig., 14 refs.

The author has plotted the iron absorption curves as determined in 30 patients at the Wellington Hospital, New Zealand, of whom 24 had hypochromic and 6 normocytic normochromic anaemia associated with various disorders. The fasting serum iron levels were estimated and after administration of 18 grains (1·2 g.) of ferrous sulphate in a single dose by mouth (or 4 mg. per kg. body weight for smaller patients and children) the serum iron content and iron-binding power were again determined at intervals of 2, 4, and 6 hours.

The patients could be divided into three groups according to their absorption curves. In Group 1 (12 patients) the serum iron level showed a sharp rise to about 400 μg. per 100 ml. within 4 hours of the dose of ferrous sulphate; all these patients had hypochromic anaemia as a result of haemorrhage and responded well to treatment. In Group 2 (2 patients) the rise in serum iron level was less marked, being between 200 and 300 μg. per 100 ml. at 4 hours, and the absorption curves just above those in normal subjects; these patients were also anaemic owing to chronic haemorrhage and required blood transfusion. In Group 3 (16 patients) the iron absorption curve was normal or below normal. This group was further subdivided into (*a*) 10 cases of hypochromic anaemia due to haemorrhage, haemorrhage with added infection, chronic infection, or allergic or metabolic disorders, with no evidence of bleeding; although having hypochromic anaemia as judged by the blood count these patients had normal serum iron levels and absorption curves and showed no response to oral iron therapy; (*b*) 6 cases of normochromic anaemia in which the main clinical state was either chronic infection, metabolic disorder, or carcinoma also showed poor or no response to oral iron therapy.

The author suggests that determination of the iron absorption curve can be a useful diagnostic procedure, allowing cases of apparent hypochromic anaemia to be

differentiated into those that are likely to respond to oral iron therapy and those that are not, so possibly saving several weeks of wasted time while awaiting a response to iron therapy. Patients whose iron absorption curve shows a high level of serum iron within 4 hours after the test dose are likely to respond well, providing there are no complicating factors such as infection or continued bleeding. A flat curve means poor absorption and indicates that response to oral iron is not likely to be good, although some of these cases may respond to parenteral iron; into this latter group fall all those cases in which chronic infection, metabolic disease, or carcinoma is interfering with the normal mechanism of iron absorption. *R. F. Jennison*

118. **Iron Absorption before and after Partial Gastrectomy**

M. D. SMITH and B. MALLETT. *Clinical Science* [*Clin. Sci.*] **16**, 23–34, Feb., 1957. 1 fig., 15 refs.

In a study of the absorption of iron from the alimentary tract before and after partial gastrectomy, carried out on 28 patients with peptic ulcer at the Radcliffe Infirmary, Oxford, a test dose of 5 mg. of iron labelled with 5 μc. of the radioactive isotope (^{59}Fe) was given orally as a solution of ferrous sulphate mixed with 50 mg. of ascorbic acid. Subsequently the amount of iron in the faeces was estimated and the amount not recovered was assumed to have been absorbed, this value being checked by determining the amount of labelled iron appearing in the erythrocytes. Of the 28 patients investigated before operation, 22 later underwent a partial gastrectomy of the Billroth-I or Polya type, and 21 of these were available for study at 6 weeks and again at 6 months after the operation. As these numbers were small and the period of postoperative observation relatively short a further 27 patients who had been subjected to a Polya partial gastrectomy 1 to 5 years previously were also investigated. Suitable controls were included in the investigation.

No gross impairment of iron absorption could be demonstrated after partial gastrectomy, and patients who had become anaemic had no defect of iron absorption and proved capable of augmenting their iron uptake in the manner characteristic of iron deficiency due to chronic haemorrhage. The authors conclude that impaired iron absorption is unlikely to account for the anaemia which occurs after partial gastrectomy, and suggest that occult blood loss probably plays an important part in causing the anaemia. *A. W. H. Foxell*

119. **A Family Study of Pernicious Anaemia**

S. T. CALLENDER and M. A. DENBOROUGH. *British Journal of Haematology* [*Brit. J. Haemat.*] **3**, 88–106, Jan., 1957. 7 figs., bibliography.

A detailed family history taken from 142 patients with proven pernicious anaemia attending the Radcliffe Infirmary, Oxford, showed that in the families of 27 (19%) of them 2 or more members had the disease, thus confirming earlier suggestions that the incidence of pernicious anaemia is unusually high in the relatives of patients; no case of pernicious anaemia was found in a control series. In all, 308 close relatives of the patients were available for study, with 259 subjects selected at random, but closely similar in sex and age, as controls. Not all of the subjects studied could be fully investigated, but as many as possible of the following determinations were carried out: serum cyanocobalamin level, gastric acidity (by the " diagnex " tubeless test meal method), urinary pepsinogen excretion, and degree of absorption of radioactive cyanocobalamin, while gastric biopsy specimens were also examined. The results of these investigations are presented in detail in tables and diagrams.

Both in the control subjects and in the patients' relatives there was a low incidence of achlorhydria up to the age of 40, after which age the relatives showed some suggestion of an increased incidence. The incidence of hypochromic anaemia was no greater than among the controls. Even when free acid was present in the gastric juice a macrocytosis (shown by halometry) was found more commonly among the relatives, suggesting that there is some factor other than deficient absorption of vitamin B_{12} responsible for this finding. It is possible that such macrocytosis is a manifestation of a carrier state. In only 2 cases could both parents of a patient be examined; in both instances one parent was normal and the other considered to have " larval " pernicious anaemia or a carrier state.

The evidence available does not permit of a conclusion as to the mode of inheritance of the disease. The manifestation of the genes is less than 100% and environmental factors confuse the picture; it is considered, for instance, that iron deficiency may induce gastric atrophy and so modify the development of pernicious anaemia. The findings of this study support the hypothesis that the gastric atrophy of pernicious anaemia is the primary lesion and that this leads to impaired absorption of vitamin B_{12}, while they are against the view that deficient absorption of the vitamin, resulting in histological changes in the gastric mucosa, is the primary defect. *R. B. Thompson*

120. **Blood Groups and Other Inherited Characters in Pernicious Anaemia**

S. T. CALLENDER, M. A. DENBOROUGH, and J. SNEATH. *British Journal of Haematology* [*Brit. J. Haemat.*] **3**, 107–114, Jan., 1957. 2 figs., 20 refs.

In the study here reported from the University of Oxford and the Lister Institute, London, the blood group of 264 patients with proven pernicious anaemia was determined. The patients included 106 males and and 158 females (ratio 1:1·5), this difference in sex incidence being apparent, however, only in the older age groups.

Tests for blood groups ABO, MNSs, P, Rh, Lewis, Lutheran, Kell, and Duffy revealed no correlation with the presence of pernicious anaemia. Only on pooling the results of ABO tests with those of other workers was a significant excess of patients with blood of Group A demonstrable. Ability to taste phenylthiocarbamide was also tested for, but again no association with pernicious anaemia was shown. There was, however, a significantly

increased incidence of persons with blue or light-coloured eyes among patients with pernicious anaemia, but no correlation could be found between freedom or attachment of the ear lobes and the disease. Further investigation is suggested into the finding of an excess of Le^a-positive erythrocytes and non-secretors to saliva inhibition tests among female patients of Lewis blood group with pernicious anaemia. *R. B. Thompson*

121. **Acute Haemolytic Anaemia with Distortion and Fragmentation of Erythrocytes in Children**
A. C. ALLISON. *British Journal of Haematology* [*Brit. J. Haemat.*] 3, 1–18, Jan., 1957. 4 figs., bibliography.

The author describes the cases of 9 children seen at the Radcliffe Infirmary, Oxford, all of whom were suffering from acute haemolytic anaemia associated with contraction, distortion, and fragmentation of the erythrocytes. Such cases fall into three distinct groups, the first two showing Heinz inclusion bodies and occurring in newborn and premature infants, while the third type affects older infants and children, without Heinz-body formation.

In the author's first case the condition was probably due to a congenital abnormality in erythrocyte metabolism; splenectomy was of no avail. A deficiency of erythrocyte catalase is postulated. The disorder is sometimes associated with multiple congenital abnormalities. The second type of syndrome comprises haemolytic anaemia with Heinz-body formation and occurs in premature newborn infants. In the author's 2 cases the disorder was attributed to overdosage with " synkavit ", a synthetic water-soluble analogue of vitamin K. In one of these 2 cases kernicterus was found at necropsy. This type of the disorder, however, is not always fatal. In the third group (6 cases) a haemolytic syndrome with erythrocyte fragmentation was associated with thrombocytopenia and renal symptoms. These cases seem to be closely related to thrombotic thrombocytopenic purpura, for platelet thrombi were found at necropsy, being especially frequent in the kidneys. Unlike thrombocytopenic purpura, however, this third type is not necessarily fatal, since 4 of the author's 6 patients recovered. *R. B. Thompson*

122. **Autoimmune Hemolytic Anemia. I. Analysis of Hematologic Observations with Particular Reference to Their Prognostic Value. A Survey of 57 Cases**
W. H. CROSBY and H. RAPPAPORT. *Blood* [*Blood*] 12, 42–55, Jan., 1957. 2 figs., 13 refs.

Autoimmune haemolytic anaemia (A.H.A.) is defined as a condition in which " the body by some unknown mechanism produces antibodies against its own erythrocytes ". Although comparatively rare, it usually presents a serious clinical problem. In this series of 57 cases, representing all those recorded in the files of the U.S. Armed Forces Institute of Pathology, Washington, D.C., between 1944 and 1954, 34 were considered to be idiopathic and 23 symptomatic, 16 being secondary to malignant disease (chronic lymphatic leukaemia, Hodgkin's disease, lymphosarcoma, reticulum cell sarcoma, or malignant lymphoma) and the other 7 to non-malignant conditions (infectious mononucleosis, Felty's syndrome, sarcoidosis, or lupus erythematosus).

Statistical analysis of the 57 cases by age and sex was of little value because of the selected nature of the population, but nevertheless the results tended to suggest that the incidence of A.H.A. symptomatic of malignant disease increased and of A.H.A. symptomatic of other conditions decreased with increasing age, while idiopathic A.H.A. occurred less frequently in the young. There was a definite seasonal increased incidence of haemolytic crises during the winter months. A postal follow-up inquiry revealed that 18 of the patients with idiopathic A.H.A. and one of the 7 with A.H.A. symptomatic of non-malignant conditions had died, but 2 of the patients with A.H.A. symptomatic of malignant disease were still living in January, 1956. In 10 cases the onset of malignant disease and that of haematological disease seemed to be almost simultaneous. A higher mortality was associated with severe anaemia, reticulocytopenia, thrombocytopenia, and leucopenia, but the presence of spherocytosis and erythroblastosis seemed to have no prognostic significance with regard to mortality. In several cases thrombocytopenia was associated with thrombo-embolic disease. Splenectomy had been performed in 27 of the cases with idiopathic A.H.A. with a good response in 10, fair in 7, and poor in one, while 9 of the patients died. Splenectomy was of value in some of the cases with symptomatic A.H.A. secondary to non-malignant conditions. *A. Ackroyd*

123. **Paroxysmal Nocturnal Hemoglobinuria. Atypical Manifestations Suggesting an Immunologic Disease**
W. DAMESHEK and H. FUDENBERG. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] 99, 202–208, Feb., 1957. 47 refs.

The current view of the pathogenesis of paroxysmal nocturnal haemoglobinuria is that abnormal erythrocytes are lysed as a consequence of minor deviations from the equilibrium which exists between the lytic and lysis-inhibiting factors of normal plasma. The nature of the erythrocyte defect has not been discovered. This paper describes 3 unusual cases of paroxysmal nocturnal haemoglobinuria seen at the New England Center Hospital, Boston. The first patient had a positive direct Coombs (antiglobulin) reaction which was reversed after treatment with cortisone, although neither the severity of the anaemia nor the characteristics of the paroxysmal nocturnal haemoglobinuria was affected. The second patient had, in addition to the diagnostic findings of paroxysmal nocturnal haemoglobinuria, an acid haemolysin in his serum which was active against his own and other erythrocytes as well as a high-titre cold agglutinin. After treatment with cortisone the haemolysin concentration decreased and finally it could no longer be detected; but haemolysis and the diagnostic criteria for paroxysmal nocturnal haemoglobinuria persisted. The third patient had proved myelosclerosis with myeloid metaplasia, and it is suggested that paroxysmal nocturnal haemoglobinuria may have developed in this case as a consequence of repeated blood transfusion. Thus 2 of the 3 patients had evidence of erythrocyte auto-

immunization, and in the third case iso-immunization seemed possible. The authors review the reported instances of paroxysmal nocturnal haemoglobinuria with evidence of auto- or iso-immunization. They suggest that the disease may well arise as a disorder of immunity and emphasize that the assumed fundamental defect of the erythrocyte remains unexplained.

In discussing their patient with concomitant myelosclerosis they point out that marrow hypoplasia is a recognized finding in paroxysmal nocturnal haemoglobinuria. This association should be remembered in investigating patients with atypical aplastic anaemia or with myeloid metaplasia.

The administration of the diuretic substance acetazolamide (" diamox ") to one of the 3 patients resulted in severe exacerbations of haemolysis, presumably because of the mild acidosis which it produces.

A. G. Baikie

HAEMORRHAGIC CONDITIONS

124. **Bleeding Tendency in Uremia**
J. H. Lewis, M. B. Zucker, and J. H. Ferguson. *Blood* [*Blood*] **11**, 1073–1076, Dec., 1956. 3 refs.

In the investigations described in this paper from the University of North Carolina the haemostatic mechanism was studied in 12 patients with chronic renal failure, all of whom also had some bleeding tendency. The laboratory studies included determination of the bleeding time, platelet count, platelet thromboplastin activity, platelet Factor-V activity, serum serotonin assay, and assays of prothrombin, Factor V, Factor VII, antihaemophilic globulin, and the Christmas factor. The most important result of the investigation was the finding of a depression of platelet thromboplastic activity and of Factor-V activity, these often being found even in the presence of a normal number of platelets. In some cases there was some deficiency of plasma coagulation components, namely, prothrombin, Factor VII, Factor V, or Christmas factor. *A. S. Douglas*

125. **Primary Hemorrhagic Diseases**
J. H. Lewis, J. H. Ferguson, J. W. Fresh, and M. B. Zucker. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **49**, 211–232, Feb., 1957. 1 fig., 33 refs.

This paper reports the results of a survey of a large number of patients with a bleeding tendency and a number of normal subjects in which the patients' haemostatic mechanism was examined in great detail with sound techniques. The tests included bleeding time, tourniquet test, platelet count, whole-blood coagulation time, clot retraction, fibrinolysis, prothrombin consumption, one-stage prothrombin test, and thrombin clotting time. Assays were made of prothrombin, Factor VII, Factor V, antihaemophilic globulin, Christmas factor, and fibrinogen. Platelet function was tested in relation to thromboplastic activity, Factor-V activity, clot retraction, and serotonin content. Antithrombin was assayed and a search made for inhibitors. [The original paper should be consulted for the technical details.]

Among 240 patients with a haemorrhagic tendency, 101 were suffering from a constitutional bleeding diathesis. These 101 cases were distributed as follows. (1) Vascular defects, 10 (2 with hereditary haemorrhagic telangiectasia and 8 with " pseudohaemophilia "). (2) Platelet defects, 4 (2 with constitutionally determined thrombocytopenia and 2 with a functional platelet disturbance—one with impaired ability to cause clot retraction and one with a low serotonin content). (3) Coagulation disorders, 87 (deficiencies of (*a*) antihaemophilic globulin, 52; (*b*) Christmas factor, 26; (*c*) Factor V, 4; (*d*) Factor VII, 4; (*e*) fibrinogen, 1).

A. S. Douglas

126. **The Preparation and Clinical Administration of Lyophilized Platelet Material to Children with Acute Leukemia and Aplastic Anemia**
E. Klein, S. Farber, I. Djerassi, R. Toch, G. Freeman, and P. Arnold. *Journal of Pediatrics* [*J. Pediat.*] **49**, 517–522, Nov., 1956. 1 fig., 9 refs.

It has been shown that lyophilized platelet material (L.P.M.) has a haemostatic effect and does not excessively activate coagulation *in vitro*. In this paper from the Children's Medical Center (Harvard Medical School), Boston, the authors report the results of the intravenous administration of 180 units of L.P.M. in 64 infusions to 10 patients whose ages ranged from 2 to 17 years. (One unit is the amount of platelet material obtained from one pint (454·5 ml.) of blood and averages approximately 400 mg.) The method of preparation is described.

Of the 10 patients, 7 were in the advanced stages of leukaemia, 2 others had " other malignancies ", and one had aplastic anaemia, while all had thrombocytopenia with platelet counts under 10,000 per c.mm. and had failed to respond to the usual measures for haemostasis. Only patients were included in the study whose blood-coagulation defects were referable solely to thrombocytopenia and which were known to be correctable by platelets *in vitro*. The results showed that L.P.M. corrected the deficient prothrombin consumption, as shown by tests carried out 12 hours after its administration, but the effect on bleeding was equivocal. No serious side-effects were encountered, and in particular no thromboembolic complications occurred, nor did post-mortem studies in 7 cases reveal any evidence of thrombosis or embolism. Because of the small number of cases and the preliminary nature of the study no definite conclusions are drawn. But since L.P.M. is stable and appears to retain much of the activity of platelets *in vitro*, with factors such as antifibrolysin, antiheparin, and thromboplastic generating activity, the authors suggest that it might be possible to make preparations containing these various platelet factors readily available.

D. G. Adamson

127. **A Thrombasthenic Syndrome Associated with Hyperheparinemia**
W. N. Bell and I. Imber. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 537–545, March, 1957. 2 figs., 19 refs.

Respiratory System

128. **Non-bronchospirometric Measurement of Differential Lung Function**
G. H. ARMITAGE and A. B. TAYLOR. *Thorax* [*Thorax*] **11**, 281–286, Dec., 1956. 6 refs.

Conventional bronchospirometry is known to be subject to errors and is often unpleasant for the patient. The present study was undertaken at the Queen Elizabeth Hospital, Birmingham, to determine whether reliable information on differential lung function could be obtained more easily by the measurement of the respiratory quotient (R.Q.) of samples of expired air obtained from the main bronchi and trachea during routine bronchoscopy. The percentage of the total oxygen uptake contributed by the right lung (normally 55%) is given by the formula:

$$\frac{\text{R.Q. left lung} - \text{R.Q. trachea}}{\text{R.Q. left lung} - \text{R.Q. right lung}} \times 100$$

The relative contribution to ventilation can be calculated in a similar manner. Contamination of the gas samples with room air does not affect the R.Q. values (and hence the relative oxygen uptake values), but it does invalidate any calculation of the differential contribution to ventilation.

At the end of routine bronchoscopy under local anaesthesia, catheters were placed in both main bronchi and in the trachea 10 and 20 cm. above the carina, and 5-ml. samples of gas were taken simultaneously during successive expirations (to a total of 30 to 35 ml.) into 50-ml. oiled all-glass syringes. The gas samples were analysed in a Sleigh apparatus. The analytical error was $\pm 0{\cdot}01\%$ N_2. Studies by this method were carried out on 10 patients without pulmonary disease, and 47 patients with unilateral or bilateral lung disease were studied. In 9 cases comparison was made between the results of conventional bronchospirometry and the present method and good agreement was obtained.

In patients with healthy lungs the maximum difference in R.Q. between samples from the main bronchi was found to be 0·021, with a mean of $0{\cdot}012 \pm 0{\cdot}005$. Complete mixing of the expired air streams was found to have occurred 10 cm. above the carcina. When a lung becomes entirely functionless the R.Q. values in the two bronchial samples become identical. This situation was encountered in 11 patients in whom there were independent grounds (clinical, operative, or bronchospirometric) for assuming that the diseased lung had lost all respiratory function. In the remaining 36 patients with asymmetrical lung disease R.Q. differences from 0·026 to 0·459 were encountered. When disease primarily decreases the ventilation of a lung the R.Q. on that side tends to approximate to that of venous blood (0·4 to 0·5), whereas disease primarily affecting pulmonary blood flow causes the R.Q. to rise. Thus, in general, pulmonary tuberculosis (with or without pleural involvement) and bronchiectasis give low R.Q. values on the affected side, while cystic disease, generalized emphysema, and emphysematous bullae cause a rise in the R.Q. on the affected side. *E. Keith Westlake*

129. **Respiratory Function after Pneumonectomy**
M. B. MCILROY and D. V. BATES. *Thorax* [*Thorax*] **11**, 303–311, Dec., 1956. 4 figs., 19 refs.

At St. Bartholomew's Hospital, London, respiratory function tests were performed on 10 male patients aged 39 to 63 who had undergone pneumonectomy (without thoracoplasty) for carcinoma of the lung. Eight patients were studied 8 to 11 months, one $2\frac{1}{2}$ years, and one 8 years after operation. Only one patient complained of dyspnoea before the operation, but postoperatively all had some exertional dyspnoea, although in only 3 was it severe enough to interfere with normal activities. No data from preoperative respiratory function tests were available for comparison.

Overinflation of the remaining lung—as indicated by increased functional residual capacity and a greater negative end-expiratory intrathoracic pressure—was found to be the usual, but not invariable, consequence of pneumonectomy. Despite considerable overinflation, distribution of air throughout the lung remained normal—in contrast to the impairment of intrapulmonary gas distribution found in the usual case of chronic bronchitis and emphysema. Pulmonary compliance was decreased more than would be expected for one normal lung in about half the patients. In 2 patients without evidence of overinflation dyspnoea was attributed to the fact that, for a given amount of exercise, the ventilation of the remaining lung was doubled. Only one patient was considered to have developed emphysema (high functional residual capacity, normal end-expiratory pressure, and diminished pulmonary diffusing capacity). This man was studied 8 years after pneumonectomy and had suffered repeated attacks of winter bronchitis. Thus the changes in lung function were not necessarily a consequence of pneumonectomy. *E. Keith Westlake*

130. **Atypical Pneumonia**
J. ALMEYDA. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **51**, 46–56, Jan., 1957. 8 figs., 13 refs.

In this paper from the Royal Chest Hospital, London, a study is presented of 135 cases of the syndrome of atypical pneumonia, defined as the "group of pneumonias which shows little or no response to known antibiotics". The cases were divided into two distinct groups: (1) 90 cases of aspiration pneumonia; and (2) 45 cases of virus pneumonia. In Group 1 the onset was insidious, with an upper respiratory tract infection or bronchitis preceding it. Cough, usually troublesome, was present early, but sputum appeared later in the disease and was scanty, sticky, and mucoid, and some-

times stained with blood. Pain was often present. In two-thirds of these cases there were definite signs of collapse or consolidation. The erythrocyte sedimentation rate (E.S.R.) and leucocyte count were moderately raised, especially when one pathogenic organism was isolated from the sputum. Chest radiographs showed segmental areas of consolidation and atelectasis, the appearances being less dense but more mottled than those of classic lobar pneumonia. These pneumonias were generally mild and of short duration, recovery usually being complete.

In Group 2 the onset was abrupt, with predominance of constitutional signs before the lung symptoms appeared. Physical signs were less definite. The E.S.R. and leucocyte count were usually normal. Radiologically, the shadows commonly overlapped segments, involved more than one lobe, and were often bilateral. The illness was sometimes severe, with delayed recovery and convalescence. *A. Gordon Beckett*

131. **The Treatment of Acute Friedlaender's Bacillus Pneumonia. A Continuing Problem**
L. P. JERVEY and M. HAMBURGER. *A.M.A. Archives of Internal Medicine* [*A.M.A Arch. intern. Med.*] **99**, 1–7, Jan., 1957. 10 refs.

In spite of the marked advances in recent years in the treatment of pneumococcal pneumonia Friedländer's bacillus pneumonia still presents very grave problems, with a mortality of about 50%. During the period 1939 to 1956 a total of 30 cases of acute primary Friedländer's bacillus pneumonia were admitted to the Cincinnati General Hospital. Of the 15 patients admitted before 1948, when streptomycin and the tetracycline group of drugs first became available, 11 died, and of the 15 treated subsequently, 8 died. These numbers are too small to be of any statistical significance, but reports from other sources also suggest that mortality from this disease has fallen since 1948.

Penicillin was not found to be of any value in treatment, and the authors recommend that a combination of sulphonamides, streptomycin, and the tetracycline group of drugs should be given until some more effective agent is discovered. *John Fry*

132. **The Role of Sinusitis in Bronchiectasis.** (Le role de la sinusite dans les bronchectasies)
R. M. VERSTEEGH and J. SWIERENGA. *Journal français de médecine et chirurgie thoraciques* [*J. franç. Méd. Chir. thorac.*] **10**, 581–590, 1956. 23 refs.

In 134 cases of bronchiectasis (108 in adults and 26 in children) studied at the St. Antonius's Hospital, Utrecht, the nasal sinuses were thoroughly investigated. There were 18 patients with diffuse bilateral (" constitutional ") bronchiectasis, of which 5 with Kartagener's syndrome and 7 of the remainder had sinusitis. The ordinary type of bronchiectasis without obvious local obstruction, usually with a history of virus infection, was present in 22 children and 85 adults; only one of the children in this group, but 34 of the adults, had sinusitis. There were 9 patients with secondary bronchiectasis due to bronchial obstruction, 3 of whom had sinusitis.

The authors discuss the difficulty of the radiological diagnosis of sinusitis and show that even with the help of clinical data the opinions of two independent observers differed in 9% of the cases. Despite this the authors believe that their diagnosis was correct and emphasize that whereas in the constitutional type of bronchiectasis sinusitis is commonly found, it is uncommon in the secondary type. The fact that it is common in adults and uncommon in children is the chief reason for the authors' conclusion that the sinusitis is secondary to the bronchiectasis. Further, sinusitis occurred only in patients with a profuse purulent sputum, and while treatment of the sinusitis before treatment of the lungs was generally unsuccessful, after treatment of the bronchiectasis the sinusitis either resolved spontaneously or responded well. *C. M. Fletcher*

133. ***Klebsiella* in Respiratory Disease**
W. WEISS, G. M. EISENBERG, A. SPIVACK, J. NADEL, H. L. KAYSER, S. SATHAVARA, and H. F. FLIPPIN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **45**, 1010–1026, Dec., 1956. 6 figs., 27 refs.

In an investigation carried out at Philadelphia General Hospital the prevalence of *Klebsiella* organisms in the sputum and bronchial secretions of 200 healthy individuals and of 97 patients without and 388 with respiratory disease was studied. The authors' conception of the genus *Klebsiella* is carefully defined according to the criteria of Kauffmann, and includes both *Klebsiella pneumoniae* and *Aerobacter aerogenes*. The incidence was 2% in healthy persons, 8·2% in patients without respiratory disease, 13·7% in patients with respiratory disease, and 23·2% in patients with respiratory disease in the medical wards. Over a 30-month period only 22·5% of the strains of *Klebsiella* could be typed with sera for capsular Types 1 to 10. The lower types, which were less common, were more frequently associated with destructive lung disease (lung abscess and atelectasis) than the higher types, and were found in no patients without respiratory disease. Of the strains isolated, 93% were susceptible to streptomycin, chloramphenicol, or both. Among 43 patients with *Klebsiella* in the sputum for whom serial culture results were available both before and during antibiotic therapy were 7 in whom *Klebsiella* appeared for the first time during treatment with streptomycin or broad-spectrum antibiotics; these strains usually were not of Types 1, 2, or 4.

The authors conclude that (1) *Klebsiella* can be present as a normal commensal in the respiratory tract; (2) its pathogenic role is difficult to substantiate except in cases which fail to respond to penicillin and subsequently respond to streptomycin or chloramphenicol; and (3) the latter drugs, either alone or in combination, represent the treatment of choice for cases of infection due to *Klebsiella pneumoniae*. *Denis Abelson*

134. **Carbonic Anhydrase Activity in Blood of Patients with Chronic Respiratory Disease**
T. H. SHEPARD. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 162–166, Feb., 1957. 3 figs., 10 refs.

Endocrinology

135. **Further Observations on the Endocrine Aspects of Argentaffinoma**
A. N. SMITH, L. M. NYHUS, C. E. DALGLIESH, R. W. DUTTON, B. LENNOX, and P. S. MACFARLANE. *Scottish Medical Journal* [*Scot. med. J.*] **2**, 24–38, Jan., 1957. 7 figs., 33 refs.

In continuation of a previous paper (*Scot. med. J.*, 1956, **1**, 148; *Abstracts of World Medicine*, 1956, **20**, 377) the authors, writing from the Western Infirmary, Glasgow, and the Postgraduate Medical School of London, report further findings in 7 cases of argentaffinomatosis in which there was an increased excretion of 5-hydroxytryptamine (5-HT). They point out the value of estimating the urinary 5-hydroxyindole-acetic acid (5-HIAA) in the diagnosis of this condition; thus while normal adults excrete from 5 to 10 mg. per day, patients with argentaffinomatosis may excrete up to 600 mg. per day. Further, measurement of the urinary 5-HIAA excretion may give some evidence of the degree of activity of the tumour. Since the essential amino-acid trytophan is used by the tumour in its production of 5-HT, a restriction of intake of protein may result in tryptophan deficiency with a resulting deficiency of nicotinic acid, which is derived from trytophan; one of the authors' patients did in fact show signs of nicotinic-acid deficiency. 5-HT appears to have an antidiuretic effect, reducing the high urinary output in 2 cases to 800 ml. per day.

In further studies the authors investigated in these patients the gastric function, the skin reaction to intradermal injection of 5-HT, the effect of reserpine, disulfiram, and histamine on the release of 5-HT, and the action, if any, of brominated lysergic acid as a 5-HT antagonist; they also determined the steroid excretion, basal metabolic rate, tumour 5-HT content, the frequency of heart lesions, and the response to Sjoerdsma's urinary screening test. It is suggested that 5-HT has no normal role as a circulating hormone and that it is normally destroyed by amine-oxidase and platelet adsorption. Most probably the syndrome of flushing, cyanosis, abdominal colic, diarrhoea, and cardiac lesions (especially pulmonary stenosis) seen in these patients is the result of excessive production of 5-HT. The condition differs from other endocrine disorders in that they represent either over- or under-stimulation of a normal physiological process, whereas this has no normal counterpart and is entirely pathological. The surgical removal of metastases is the most effective treatment at present and especially important in view of the effect of the tumour on the heart. *G. S. Crockett*

136. **Effect in Women of Bilateral Oophorectomy on Circulating Thyroid Hormone**
F. J. STODDARD, W. W. ENGSTROM, W. F. HOVIS, L. T. SERVIS, and A. D. WATTS. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **17**, 561–564, April, 1957. 2 figs., 8 refs.

PITUITARY GLAND

137. **Chromophobe Adenoma of the Pituitary Gland. A Follow-up Study on 60 Surgical Patients with Special Reference to Endocrine Disturbances.** [In English]
E. F. MOGENSEN. *Acta endocrinologica* [*Acta endocr. (Kbh.)*] **24**, 135–152, Feb., 1957. 23 refs.

The author discusses the follow-up results in 60 cases of chromophobe adenoma operated on at the Kommune Hospital, Aarhus, Denmark, during the years 1943 to 1954. The series, which represents an incidence of 2 to 3 cases annually per million of the population, consisted of 30 male and 30 female patients, two-thirds of whom were over the age of 40, the youngest being a girl of 13 years and the oldest a man of 68. The main indications for operation were enlargement of the sella turcica and restriction of the visual fields; in 5 cases a second operation for recurrence was performed. The over-all operative mortality was 11% (7 deaths). The tumour was cystic in 6 cases and solid in the remainder. Radiotherapy was given postoperatively to 10 patients because of the frequency of mitosis observed in the histological sections of the removed tumour tissue, but in spite of this there was recurrence of the growth in 2 of the patients.

Of the 53 patients followed up for varying periods from one to 14 years, 3 died with recurrences during the period of observation and 47 of the 50 survivors were readmitted to hospital for assessment. The mortality was highest among cases with the greatest visual loss. After operation vision improved in 29 and was worse in 13, but none went completely blind. There was some correlation between visual acuity and optic atrophy. No patient had papilloedema. Preoperatively 9 of the men and 4 of the women had reduced endocrine function, most of them showing the classic features of hypopituitarism, the manifestations of which were more marked in the younger men. One man had several features of Cushing's syndrome, another sexual precocity, and one female patient had had acromegaly for 5 years. In only a few of the cases, however, was there any biochemical evidence of depressed adrenal or thyroid function.

Depressed gonadal function, as a result of pressure on either the pituitary or the hypothalamus, was probably present in about one-quarter of the men and in almost all of the women, amenorrhoea generally occurring early in the disease. Fertility was lower than normal. After operation more than half of the men were thought to be hypocrine, but the proportion of women so affected was only slightly increased. Gonadal function was reduced in two-thirds of the men and in all but one of the women. Biochemical evidence of depressed adrenal function was now manifest in half of the patients, whereas diminished thyroid function was present in only just under one-third. Diabetes insipidus occurred in one case and acute adrenal

insufficiency in 2. Of the 47 men and women seen post-operatively 33 were back in their former employment, but 6 were totally incapacitated, 3 as a result of decreased pituitary function and one because of poor vision.

With regard to substitution therapy, which is most often required for gonadal deficiencies, the author suggests that although chorionic gonadotrophins were employed in this series with success, caution should be exercised in starting androgenic substitution therapy in patients with mild sexual difficulties, since there is some evidence that recurrence is induced by such treatment. He administers adrenocortical hormones only when symptoms are relatively severe and deficiency of the hormones confirmed by laboratory tests. He also points out that before hypothyroidism is treated, adrenocortical function should be studied since in some cases acute adrenal failure has been induced by thyroid treatment.

A. Gordon Beckett

138. **Treatment of Hypopituitarism**

R. N. BECK and D. A. D. MONTGOMERY. *British Medical Journal* [*Brit. med. J.*] **1**, 441–444, Feb. 23, 1957. 1 fig., 9 refs.

The therapeutic control of patients with pituitary insufficiency is usually satisfactory provided replacement of adrenal hormone is carried out. Some workers have claimed excellent results from the use of cortisone alone: others advocate a wider range of substitution therapy and include deoxycortone acetate, testosterone, and thyroid extract in addition to cortisone. The present authors report, from the Royal Victoria Hospital, Belfast, their observations on 4 female out-patients suffering from postpartum pituitary insufficiency who were treated for periods ranging from 8 to 20 months on a combined regimen consisting of deoxycortone acetate, sodium chloride, methyltestosterone, stilboestrol, thyroid, and cortisone, followed subsequently for periods of 7 to 11 months by cortisone alone. Each patient was assessed at three stages: (1) before treatment started, (2) when combined therapy was withdrawn, and (3) at the end of the trial period on cortisone, the following points being considered at each assessment: energy and capacity for work, emotional tone and mental state, libido, menstruation, incidence and severity of infections and crises, tolerance to cold, blood electrolyte level, blood pressure, weight, any effects on the skin and hair, and finally changes in the electrocardiogram (ECG).

Profound weakness and depression were characteristic of all the cases before treatment. In all, however, there was a remarkable recovery as a result of the combined treatment, although one patient suffered a recurrence of asthenia, which disappeared when treatment with thyroid was reinstituted. The depression also cleared up and a normal mental state was restored in all cases, thyroid being required in one. Libido had been absent in all the patients and was only fully restored in one, in whom it was maintained equally well with either combined therapy or cortisone alone. Amenorrhoea was a feature of the illness in all 4, but in 3 cases a 3- or 4-day period was established by means of intermittent stilboestrol therapy; complete amenorrhoea followed when stilboestrol was withheld. All the patients complained of intolerance to cold, but this disappeared with the combined therapy and the improvement was maintained in 3 cases with cortisone alone and in the fourth with cortisone and thyroid. Electrolyte balance and blood pressure were maintained equally well by combined therapy or by cortisone alone. The electrocardiographic changes characteristic of myxoedema were present in 3 cases before treatment, and although there was an improvement with combined therapy, some regression occurred after changing to cortisone.

Discussing their findings the authors consider that thyroid and cortisone were the only substances which played a significant part in the remission of the symptoms of hypopituitarism. Furthermore, cortisone alone was found to be inferior to combined therapy only in respect of controlling the depression and intolerance to cold in one case and in preventing ECG changes in 2 and minor skin changes in 2, all these being related to the withdrawal of thyroid, since they quickly improved when this hormone was again administered. It is concluded that while cortisone alone seems to be little inferior to combined therapy the routine use of thyroid is also desirable, but in the authors' opinion deoxycortone acetate, additional sodium chloride, and testosterone are not necessary as a routine.

John Lister

THYROID GLAND

139. **Metabolic Studies in Myxedema following Administration of L-Triiodothyronine: (1) Duration of Negative Nitrogen Balance; (2) Effect of Testosterone Propionate; (3) Comparison with Nitrogen Balance in a Healthy Volunteer**

K. R. CRISPELL, G. A. WILLIAMS, W. PARSON, and G. HOLLIFIELD. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **17**, 221–231, Feb., 1957. 4 figs., 10 refs.

Metabolic studies were carried out at the University of Virginia Hospital, Charlottesville, on 2 myxoedematous patients following administration of 100 μg. of L-triiodothyronine daily by mouth for 220 days and 101 days respectively. The first patient, a man of 43, was in positive nitrogen balance before treatment started, while the second patient, a woman of 31, was in nitrogen equilibrium. In both instances the nitrogen balance became negative within 24 hours of the first dose of the drug, and remained negative for the whole period, although it was greater (-3 to -6 g.) during the first few weeks than later (-1 to -2 g. daily). During the first 6 weeks of treatment the patients lost weight and excreted excess urine, but the basal metabolic rate and serum cholesterol concentration became normal. Thereafter the patients were apparently in normal thyroid equilibrium, although the nitrogen loss continued, this loss being prevented in the male without affecting the thyroid state by administration of 25 mg. daily of testosterone propionate. A healthy subject given the same dose of L-triiodothyronine for 10 days showed a much smaller (probably insignificant) nitrogen loss.

Peter C. Williams

140. **The Infrequency of Myocardial Infarction in Patients with Thyrotoxicosis**

D. S. LITTMAN, W. A. JEFFERS, and E. ROSE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 10–15, Jan., 1957. 17 refs.

In this paper from the Hospital of the University of Pennsylvania, Philadelphia, and the Veterans Administration Hospital, Wilmington, Delaware, the authors set out to demonstrate that myocardial infarction rarely occurs in acute thyrotoxicosis. After reviewing some of the literature on the association of angina of effort and thyrotoxicosis and on serum lipid metabolism in thyroid dysfunction, in which they were able to find only one authentic case of myocardial infarction occurring in active hyperthyroidism, they report 3 cases in which both conditions occurred together. The first patient, a man of 52 without any history of angina, developed an acute myocardial infarction during a recurrence of thyrotoxicosis 6 years after undergoing subtotal thyroidectomy. The second patient, a negress of 51, also without a history of angina, suffered myocardial infarction during operation for subtotal thyroidectomy. The third patient, a man of 37, had exophthalmos with a diffusely enlarged thyroid gland; a routine electrocardiogram revealed evidence of recent infarction. The patient died shortly afterwards, and at necropsy atherosclerosis of the left coronary artery with thrombotic occlusion of the right coronary artery was found.

The authors suggest that there may be a correlation between the serum lipoprotein concentration and the incidence of myocardial infarction in patients with active thyrotoxicosis, although this was not studied in any of the present cases. *Gerald Sandler*

141. **The Effect of Thyroid Ablation upon Serum Cholesterol and β-Lipoprotein Spectrum**

W. H. FLORSHEIM, M. E. MORTON, and J. R. GOODMAN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 16–22, Jan., 1957. 20 refs.

The changes in the serum cholesterol and β-lipoprotein levels after administration of radioactive iodine (^{131}I) were studied at the Veterans Administration Hospital, Long Beach, California, and the University of California Medical School, Los Angeles, in 3 groups of patients: (1) hyperthyroid patients rendered euthyroid, (2) patients subjected to total removal of the thyroid gland for cardiac insufficiency due to atherosclerotic heart disease, and (3) patients subjected to surgery as in (2) but for other reasons—for example, cor pulmonale. The patients were followed up for periods of 6 to 44 months. Thyroid function was assessed from the uptake of ^{131}I by the thyroid gland, the results of the thyroxine synthesis test, the serum protein-bound iodine level, and the basal metabolic rate. After stabilization of thyroid function, a non-myxoedematous hypometabolic state was maintained by thyroid medication, when necessary.

In the hyperthyroid group the increase in the serum cholesterol level was below 25%, except in 2 patients rendered hypothyroid, and the changes in the β-lipoprotein pattern were confined almost entirely to the S_f 0–12 class. Thus there was only a minimal increase in Gofman's " atherogenic index ". In Group 3 (without atherosclerotic heart disease) changes in the serum cholesterol level were negligible after optimum stabilization at a hypometabolic level; changes in the β-lipoprotein pattern were confined to the S_f 0–12 class and did not exceed 25%, so the " atherogenic risk " was again not increased. In Group 2 (with atherosclerotic heart disease) two-thirds of the patients had dramatic relief of anginal pain, but the biochemical changes were more variable. In some instances changes were minimal, but in others there were increases in both the cholesterol and β-lipoprotein levels in the serum (the latter not confined to the S_f 0–12 class), with a definite increase in the " atherogenic index ". The authors suggest that this increase may be the result of the well-known periodic progression of atherosclerosis, and not related to total removal of the thyroid gland. They conclude that the clinical relief obtained in these cases is worth any added slight risk of increased atherogenesis.

Gerald Sandler

142. **Treatment of Hyperthyroidism with Individually Calculated Doses of I^{131}**

F. K. BAUER and W. H. BLAHD. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **99**, 194–201, Feb., 1957. 2 figs., 21 refs.

The results of the treatment of 106 hyperthyroid patients with radioactive iodine (^{131}I) are analysed in this paper from Wadsworth General Hospital (University of California School of Medicine), Los Angeles. The diagnosis of hyperthyroidism was confirmed by determination of the serum protein-bound iodine level, basal metabolic rate, serum cholesterol content, and uptake of radioactive iodine. The tracer dose of ^{131}I was 2 μc., which was given in a capsule after breakfast, subsequent uptake by the thyroid gland at a distance of 10 cm. being measured at intervals of 6 and 24 hours. The weight of the thyroid gland was estimated from the " scintigram " (obtained after estimation of the effective half-life of the tracer dose), the measured area of the gland as outlined on the neck being multiplied by the mean length of the two lobes and by a factor of 0·321 to account for volume. This method showed that the initial gland weight ranged from 15 to 151 g.; the therapeutic dose of ^{131}I was calculated according to Quimby's formula, which is based on the weight of the gland in grammes multiplied by 8 (the physical half-life of ^{131}I) divided by the effective half-life of the dose of ^{131}I in days, multiplied by the maximum percentage uptake. Repeat tracer doses of ^{131}I were given at intervals after therapy, 50 of the patients requiring two or more doses of the isotope.

Of the 106 patients treated by this method, 100 (94·3%) were clinically euthyroid within 3 to 5 months after institution of therapy. Only one patient had a recurrence of hyperthyroidism after a 3-year period of euthyroidism, but 6 of the patients (5·7%) developed permanent hypothyroidism. Other complications noted were exophthalmos (one case), gynaecomastia and acne (13 cases), and pretibial myxoedema (one case). Patients with pre-existing heart disease due either to thyrotoxicosis alone or to this and superimposed organic heart

disease became much easier to control after treatment. Although 18 of the patients became clinically euthyroid, yet laboratory tests showed that they were still within the hyperthyroid range. Contrary to the experience of other workers the treatment had a bad effect on myasthenia gravis, present in 2 of the patients, one of whom subsequently died in a respirator.

[The original paper should be consulted for the exact method of determining the dosage.]

I. McLean Baird

143. **The Thyroid-stimulating Hormone (TSH) Test. An Aid to the Differential Diagnosis of Nontoxic Disease of the Thyroid**

P. G. SKILLERN and B. R. EVANS. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **99**, 234–244, Feb., 1957. 4 figs., 37 refs.

It has been shown that in patients with normal thyroid function a single intramuscular injection of thyroid stimulating hormone (T.S.H.) causes an increase in the rate of uptake of radioactive iodine (^{131}I) by the thyroid gland, the increase being maximum after 24 hours. In this paper from the Cleveland Clinic, Cleveland, Ohio, the authors describe the results obtained after administration of 4 units of T.S.H. in patients with various non-toxic thyroid diseases. There was an increase in the ^{131}I uptake in all of 32 euthyroid patients, in 25 out of 29 such patients taking desiccated thyroid tablets, and in all of 31 patients with non-toxic adenomatous goitre. The response to this test was abnormal and did not cause an increase in uptake of ^{131}I in 17 patients with primary hypothyroidism and 30 out of 31 patients with struma lymphomatosa (Hashimoto's disease). Abnormal results were also obtained in 4 out of 11 patients with anterior pituitary failure without primary hypothyroidism, there being an increase in ^{131}I uptake after administration of T.S.H. in the remaining 7 patients in this group.

The test was most useful for differentiating the euthyroid condition from mild hypothyroidism and struma lymphomatosa from non-toxic adenomatous goitre. The basis of the test and the reasons for its occasional failure in the differentiation of hypothyroidism from hypopituitarism are discussed.

I. McLean Baird

144. **A Long-term Follow-up of Nontoxic Nodular Goiter. Effect of Clinical Selection on the Observed Incidence of Malignancy**

J. E. SOKAL. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **99**, 60–69, Jan., 1957. 1 fig., 19 refs.

A long-term follow up is reported of 296 patients at the Grace–New Haven Community Hospital, New Haven, Connecticut, in whom nodular goitre or cancer of the thyroid gland was diagnosed between the years 1921 and 1945.

Patients were divided into three groups: (1) 140 patients who were not operated on within 6 months of diagnosis of non-toxic nodular goitre; (2) 80 patients in whom local removal of adenomata was undertaken; and (3) 83 subjected to thyroid lobectomy or thyroidectomy, excluding those in whom malignancy was definitely diagnosed before operation. The over-all ratio of females to males was 5:1. Only one patient in Group 1 was later found to have cancer of the thyroid; in Group 2 there were 2 cases in which the excised nodule was found histologically to be malignant; while in Group 3 there were 13 patients (16%) with proved malignant goitre, the growth being metastatic in one case and primary in the others.

The author considers that these figures demonstrate impressively the value of preoperative selection, and that a policy of removing as a routine all non-toxic thyroid nodules because of the danger of malignancy is not justified.

Denis Abelson

PARATHYROID GLANDS

145. **The Signs of Parathyroid Involvement in 17 Cases of Osteomalacia.** (Les signes de participation parathyroïdienne dans 17 cas d'ostéomalacie)

S. DE SÈZE, A. LICHTWITZ, D. HIOCO, P. BORDIER, and A. MAZABRAUD. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **72**, 1007–1017, Dec. 7, 1956. 3 refs.

At the Hôpital Lariboisière, Paris, 17 cases of idiopathic osteomalacia were selected for biochemical investigation, the diagnostic criteria adopted being: (*a*) the presence of one or more Milkman's pseudofractures, (*b*) the presence of osteoid tissue on histological examination, (*c*) a persistent hypocalciuria (less than 70 mg. daily on average), with a diminution in the product of the serum calcium and phosphate levels [presumably in mg. per litre] to below 2,800 (normal $3{,}200 \pm 400$), and (*d*) characteristic findings on administration of calcium intravenously and of calciferol by mouth. Most of the patients were found to be in negative calcium balance, with a high faecal calcium content, the serum calcium level being reduced. The phosphate level was slightly reduced in both serum and urine, with an elevated urine: serum ratio. In general, the greater the reduction in serum phosphate level, the more nearly normal was the serum calcium level.

The authors conclude that their findings suggest that hyperparathyroidism is a factor in idiopathic osteomalacia.

Allene Scott

146. **Exploratory Biological Tests of Parathyroid Activity in Cases of Osteomalacia.** (Épreuves biologiques d'exploration des parathyroïdes chez les ostéomalaciques)

S. DE SÈZE, A. LICHTWITZ, D. HIOCO, P. BORDIER, and A. MAZABRAUD. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **72**, 1018–1029, Dec. 7, 1956. Bibliography.

To test the hypothesis that hyperparathyroidism is a factor in the pathogenesis of osteomalacia [see Abstract 145] three methods were utilized in the investigation of a group of 17 patients with this disease. (1) Calcium gluconate in a dosage of 13·2 mg. Ca per kg. body weight in 500 ml. of normal saline was administered intravenously over a 3-hour period. In contrast to the

marked elevation of the serum phosphate level which normally follows this procedure these patients showed a delayed response, with only a slight increase. (2) Administration of vitamin D_2 (calciferol) resulted in accentuation of the hypocalciuria and an elevation of the serum phosphate level, but no increase in urinary phosphate content. (3) Punch biopsies of marrow-containing bones were taken and showed much osteoid tissue with osteoclasts and collagen proliferation in the medulla.

It was found that the results of all these tests in the patients suffering from idiopathic osteomalacia closely paralleled those obtained in cases of primary hyperparathyroidism. *Allene Scott*

147. **An Attempt to Interpret the Relationship between Osteomalacia and Hyperparathyroidism.** (Essai d'interprétation des rapports entre ostéomalacie et hyperparathyroïdie)
S. DE SÈZE, A. LICHTWITZ, D. HIOCO, P. BORDIER, and A. MAZABRAUD. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] 72, 1029–1035, Dec. 7, 1956. 4 refs.

The syndromes of primary osteomalacia and primary hyperparathyroidism are here envisaged as two components of the same adaptive response, the former serving to protect the bones from total destruction, while the latter preserves neuromuscular function in the face of hypocalcaemia. In contrast to the so-called secondary forms of osteomalacia due to poor dietary intake of calcium, to malabsorption resulting from gastro-intestinal disease, or to phosphorus retention in renal disorders, the primary type responds to a high dosage of calciferol administered over a long period. However, there is no clinical evidence in such cases of hypovitaminosis D, and the dosage necessary for the treatment of primary osteomalacia is far greater than that required to cure rickets or osteomalacia secondary to malnutrition. Moreover, the effect of such treatment is to provoke signs suggestive of hypoparathyroidism, and the authors therefore suggest that vitamin D_2 reduces an excessive parathyroid activity which is the main cause of decalcification in primary osteomalacia.

It is pointed out that in the primary form of hyperparathyroidism there is compensatory osteoblastic activity as well as osteoclasis. Hence if the disease develops as a continuous process, then osteoclastic effects will be predominant, but if it develops intermittently the main features will be osteoblastic, the osteoclasts disappearing rapidly after each bout whereas the osteoblasts survive for several months. It is suggested that such osteoblastic preponderance is the explanation of the usual findings in the most common form of hyperparathyroidism, that is, marked biochemical changes indicating osteolysis but with few visible bony lesions and with a histological picture resembling that of osteomalacia.

Thus in each syndrome there exist features that are suggestive of the other, and further investigations should be carried out to elucidate the question of their true relationship. *Allene Scott*

ADRENAL GLANDS

148. **Effect of Prednisone and Prednisolone on Antibody Formation in Mice**
E. J. FOLEY, W. A. MORGAN, and G. GRECO. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] 7, 70–74, Feb., 1957. 15 refs.

It has been shown that cortisone and hydrocortisone suppress antibody formation. It has also been shown that the newer steroids, prednisone and prednisolone, are 3 to 5 times more active than cortisone or hydrocortisone in animal experiments and also in anti-arthritic potency in human subjects. Experiments were therefore carried out to determine whether the newer steroid compounds had any greater effect than cortisone in suppressing antibody formation. In mice antibodies were produced against antigens and erythrocytes and the influence of various amounts of steroids was studied, the effect of cortisone being compared with that of prednisone and of prednisolone. The formation of bacterial and erythrocyte agglutinins was impaired to some extent when large doses (25 mg. per kg. body weight) of these steroids were given during the course of antigen injections; this also occurred, but to a lesser extent, when the dose of the 3 steroids was 5 mg. per kg. It was also found that very large doses of cortisone and of prednisone (50 mg. per kg. per day) prevented the development of immunity to C3H lymphosarcoma in mice; this was not observed when a dose of 5 mg. per kg. was given.

No evidence was adduced that prednisone or prednisolone interfered with antibody formation or the development of foreign-tissue immunity to a greater extent than did cortisone. The authors consider this to be of some importance, since roughly 4 times more cortisone than prednisone or prednisolone is required for anti-arthritic effect in human beings. *R. F. Jennison*

149. **The Role of the Adrenals in the Production of Renal Changes by STH**
H. SELYE and P. BOIS. *Journal of Urology* [*J. Urol. (Baltimore)*] 77, 1–11, Jan., 1957. 8 figs., 12 refs.

It has been shown previously in experimental animals that certain effects of the " growth hormone " or somatotrophic hormone (S.T.H.), namely, those on the kidney and cardiovascular system, are dependent upon the presence of the adrenal glands, in contrast to the effects on skeletal growth and the lymphatic system, which occur in the absence of these glands. In this paper from the University of Montreal the authors report further experiments on the nephrotoxic effect of S.T.H. in rats and the possible participation of the adrenomedullary hormone in the mechanism. Female Sprague-Dawley rats were optimally " conditioned " for nephrotoxic hormone action (by unilateral nephrectomy and supplements of sodium chloride) and were then subjected to total adrenalectomy, life being maintained by administration of deoxycortone acetate and in some cases cortisol acetate (COLA) as well. One group of rats received adrenaline and noradrenaline (200 μg. daily) by subcutaneous injection, while 1·5 or 2 mg. of S.T.H. in aqueous solution was injected subcutaneously twice daily.

The fluid intake of the animals was measured daily as an indicator of the polyuria which is a characteristic sign of hormonally-produced nephrosclerosis. The animals were killed after 21 days, and the organs were weighed and histologically examined.

The results showed that in the absence of functioning adrenal tissue S.T.H. did not cause kidney or cardiovascular damage, even in the presence of adequate doses of deoxycortone or cortisol acetate, adrenaline, and noradrenaline. Moreover, the effects upon the kidney of nephrotoxic amounts of the corticoids alone could not be aggravated by simultaneous administration of S.T.H. The authors suggest that under the influence of this hormone deoxycortone acetate or a closely similar compound is transformed into a more active corticoid, which has a nephrotoxic effect. *Nancy Gough*

150. **Effect of Cortisone on the Abnormal Distribution of Intravascular Water in Adrenal Cortical Insufficiency in Man**

J. F. DINGMAN, D. H. P. STREETEN, and G. W. THORN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **49**, 7–18, Jan., 1957. 2 figs., 16 refs.

In this communication from the Peter Bent Brigham Hospital, Boston, the authors advance the theory that the delayed diuresis which occurs after a water load in patients with Addison's disease is due to abnormal distribution of the ingested water in the body rather than to faulty renal response. To test this hypothesis they investigated the changes in the water content of plasma and erythrocytes, calculated from changes in the haemoglobin concentration and in the haematocrit, after a conventional Robinson–Power–Kepler water-excretion test in normal subjects and treated and untreated patients with adrenocortical deficiency.

The test showed that in 13 healthy subjects there was a hypotonic expansion of the plasma volume with a transient increase in erythrocyte hydration until diuresis occurred during the 2nd hour after the ingestion of the water load. The erythrocyte volume then rapidly returned to normal, although the increase in plasma volume persisted until after the 4th hour. In 10 patients (5 men and 5 women) with untreated Addison's disease there was a significantly greater and more persistent increase in erythrocyte water content than in the normal subjects, but plasma hydration did not differ significantly either in degree or duration from normal. The delay in water diuresis thus parallels the erythrocyte water content rather than the degree of plasma dilution.

It seems reasonable to assume that excessive hydration may also occur in other cells of the body, and the authors suggest that this abnormality in fluid distribution is the cause rather than the consequence of the delayed water diuresis in Addison's disease. The abnormality can be completely corrected by the administration of 100 to 200 mg. of cortisone, as was shown in a further group of 6 patients, and was then accompanied by a normal diuretic response to the water load. However, the erythrocytes of patients with Addison's disease exhibit no abnormal permeability to water when exposed to increasing haemodilution *in vitro*, nor does hydrocortisone have any effect on their permeability. The authors therefore suggest that the abnormal changes found *in vivo* may be related to the persisting excretion of antidiuretic hormone and that cortisone can correct the abnormality by inhibiting the secretion of this hormone. *Robert Mahler*

151. **9-*alpha*-Fluorohydrocortisone Alone and Combined with Hydrocortisone in the Management of Chronic Adrenal Insufficiency**

W. LEITH and J. C. BECK. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **17**, 280–290, Feb., 1957. 7 figs., 11 refs.

A trial of 9-α-fluorohydrocortisone alone and in combination with hydrocortisone in the management of chronic adrenal insufficiency is reported from the Royal Victoria Hospital, Montreal. In the first part of the investigation 2 patients with Addison's disease were given 1 or 2 mg. of 9-α-fluorohydrocortisone daily by mouth in place of 50 mg. daily of cortisone. With the higher dose there was retention of sodium, chloride, and water, and the serum potassium concentration fell, this last being unexplained and not due to an increase in urinary excretion of potassium. When the dosage was reduced to 1 mg. daily both patients continued to gain weight, oedema was still present, and the serum potassium level was still below normal. Similar changes were observed in a third patient with Addison's disease who was given a tablet containing 5 mg. of hydrocortisone and 0·1 mg. of 9-α-fluorohydrocortisone every 6 hours.

In the second part of the investigation 8 patients with chronic adrenal insufficiency were given 9-α-fluorohydrocortisone only. The dosage initially was 1·5 mg. daily by mouth, but because of generalized oedema this was reduced gradually to 0·5 mg. The oedema disappeared at this dosage level, but the patients complained of weakness and fatigue, and the serum potassium level still remained below normal. When treatment was changed to a combination of 5 mg. of hydrocortisone and 0·1 mg. of 9-α-fluorohydrocortisone twice daily the clinical response was excellent, the patients continuing well for a year. The serum potassium level was usually subnormal, but no symptoms of potassium deficiency were seen. The authors state that the dosage of cortisone necessary to achieve a similar effect was 37·5 mg. daily, with in addition supplements of sodium chloride.

Peter C. Williams

152. **Metabolic Response to Adrenalectomy**

R. P. JEPSON, A. JORDAN, M. J. LEVELL, and G. M. WILSON. *Annals of Surgery* [*Ann. Surg.*] **145**, 1–11, Jan., 1957. 2 figs., 15 refs.

An attempt was made at Sheffield Royal Infirmary to investigate the role of the adrenal glands in the metabolic response to operation by studying water, electrolyte, and nitrogen balance, as well as urinary excretion of 17-ketosteroids and 17-ketogenic steroids, in patients undergoing bilateral adrenalectomy and oophorectomy for mammary carcinomatosis. The 8 subjects were between the ages of 30 and 58 years and had widespread soft-tissue and often bony metastases following a previous radical

mastectomy for mammary carcinoma. A full study was made of 7 patients, 2 of whom underwent a one-stage bilateral adrenalectomy and oophorectomy, while 5 were studied during removal of the second adrenal gland some 10 to 14 days after removal of the ovaries and one gland. All these patients received cortisone throughout the study, the 5 undergoing the second adrenalectomy in doses of 200 mg. daily and the other 2 in doses of 150 and 100 mg. daily respectively, starting 3 to 12 days before the operation. (Investigations in the eighth case were limited to the blood electrolyte and eosinophil changes.)

A slight fall in serum sodium and chloride levels was noted, which was of a similar order to that seen in " normal " patients undergoing surgery. The balance data were compared with those obtained in similar studies on patients undergoing partial gastrectomy and showed the same tendency to retention of sodium and chloride and loss of potassium. Although the retention of sodium and chloride was less and the loss of potassium greater in the authors' subjects, the differences were not significant. The range of values in the nitrogen-balance studies was wide and the average loss less than has been reported in patients undergoing gastrectomy. The authors suggest that this difference may be attributed to the debilitated state of their patients and to the fact that in 5 cases there had been a previous recent operation, the negative nitrogen balance in the other 2 cases being greater than the average despite a lower dosage of cortisone. All remained in positive fluid balance. Although the excretion of ketogenic steroids before operation varied with the amount of cortisone administered, there was a wide variation, from 29 to 53·4 mg., in the mean daily postoperative output of the 5 patients who were all receiving the same dosage of cortisone and had been subjected to the same operative procedure. This variation could not be related to the patients' weight, daily urinary volume, or general condition, and it was therefore thought to be due either to individual differences of metabolic pattern or to varying ability to mobilize intramuscular cortisone. In 2 cases the eosinophil count showed no rise following a preoperative suppression by cortisone, while in the remainder it remained high before operation and was depressed for only a few days immediately after operation, after which it returned to or exceeded the preoperative level.

It was concluded that the pattern of metabolic response to trauma in these patients fell within the accepted " normal " range and therefore that variations in adrenocortical steroid levels are not essential either for the initiation or maintenance of metabolic changes after surgical operation. *B. M. Ansell*

153. **Treatment of Adrenocortical Deficiency States**
F. D. HART. *British Medical Journal* [*Brit. med. J.*] 1, 417–422, Feb. 23, 1957. 28 refs.

The author reports his experience at Westminster Hospital, London, in the treatment of 150 patients rendered deficient in adrenocortical hormone by adrenalectomy, performed in 5 cases for malignant hypertension, in 2 for Cushing's syndrome, and in 143 for metastatic malignant disease. Of the last-mentioned group of patients, 65 survived more than 6 months; the 2 patients with Cushing's syndrome remain alive and well, but only one of the 5 patients with malignant hypertension survived more than 2 years, the others dying at 10, 12, 12, and 19 months respectively after operation.

The greatest therapeutic problems arose in maintaining the patients subjected to adrenalectomy because of metastatic malignant disease, the chief variables to be studied in these cases being the salt and water balance, the cortisone requirements, and the activity of the underlying malignant disease process. The author emphasizes the difficulty in differentiating between the symptoms and signs of water and sodium imbalance and of cortisone deficiency. Thus apathy, anorexia, nausea, and vomiting may be due to water intoxication, sodium loss, or cortisone deficiency; the last may be absolute, as occurs in omission of the usual dosage, or relative, when due to intercurrent infection or extension of the malignant disease. Of the salt-retaining agents at present available, cortisone and hydrocortisone may provide adequate substitution in many cases. Aldosterone is the most potent sodium-retaining, potassium-eliminating hormone yet isolated from cortical extract, but it has been shown that in adrenalectomized man aldosterone given alone does not prevent signs of adrenal deficiency (Maclean *et al.*, *J. clin. Invest.*, 1955, **34**, 951).

Recently 9-α-fluorohydrocortisone has been found to be a more potent salt-retaining agent than hydrocortisone itself, but used alone it is too potent for practical use. However, in combination with cortisone acetate doses of 0·125 mg. of 9-α-fluorohydrocortisone may be of great value, especially in patients who are themselves able to detect early symptoms and signs of mild salt deficiency; in cases of severe salt deficiency a larger dose (1 mg.) of 9-α-fluorohydrocortisone may be required. Until this preparation became available deoxycortone acetate was a useful supplement to cortisone therapy, and liquorice root and its extracts also exert a mild deoxycortone-like action; when administered to adrenalectomized subjects in conjunction with cortisone, glycyrrhetinic acid causes some retention of sodium and chloride, but has a stronger water-retaining effect.

In the author's series of adrenalectomized patients the hypertensive group remained well on a daily dose of 50 mg. of cortisone acetate with no additional salt-retaining agent, and similarly no problem regarding salt and water balance arose in the cases of Cushing's syndrome. In the group with metastatic malignant disease, however, control was more difficult. Initially they were mostly controlled on cortisone alone in a daily dose of 50 mg., but in many cases salt deficiency developed later and additional therapy with deoxycortone acetate or 9-α-fluorohydrocortisone was required. The author stresses the importance of maintaining adrenalectomized subjects on full substitution therapy and has found that the required daily dose of cortisone ranges from 37·5 to 50 mg. In an adrenal crisis, intravenous hydrocortisone, 100 to 300 mg. in a saline infusion given over 6 to 24 hours, has proved the best treatment; for the crisis in patients with severe salt loss 9-α-fluorohydrocortisone may be infused intravenously in one-twentieth of the dose of cortisone. *John Lister*

DIABETES MELLITUS

154. **Pulmonary Tuberculosis and Diabetes Mellitus**
M. T. WARWICK. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **26**, 31–42, Jan., 1957. 3 figs., 29 refs.

The investigation described herein was based on 104 cases of diabetes with active tuberculosis, about half of which were seen at the Brompton and London Chest Hospitals and half at the Diabetic Clinic, University College Hospital, London, where tuberculosis was diagnosed. The period of observation was longer than in most previously reported studies, slightly more than half (55) of the patients having been followed up for over 5 years.

The incidence of tuberculosis was found to be 18·2 per 1,000 in diabetic subjects, compared with an "expected incidence" of 9·1 per 1,000 in the control non-diabetic population. Tuberculosis was commoner in female than in male diabetics at all ages up to 65 years. In 77 of the 104 patients diabetes was the initial disease, in 19 tuberculosis and diabetes were diagnosed simultaneously, and in 8 tuberculosis was diagnosed first. Notable features of diabetes in tuberculous patients were: (1) 62% of patients under 40 developed tuberculosis in the first 10 years of diabetic life; (2) the severity of the diabetes (defined arbitrarily in terms of insulin requirement) in patients with tuberculosis was not significantly different from that in patients without tuberculosis; (3) the degree of control of the diabetes was found to be an important factor, poor control being more common in patients who later developed tuberculosis—a history of ketosis was six times more frequent among patients who later developed tuberculosis than in those who did not. The extent of disease at the time of radiological diagnosis was usually less than that in other reported series. The wedge-shaped opacity in which there is cavitation, the so-called typical lesion described by others, was observed in very few instances, and the author found no evidence to support the view that it was characteristic of tuberculous diabetics.

The patients were divided into two groups—those whose treatment finished before 1950 and therefore did not have antibacterial drugs, and those treated after that date. There was little difference between the two groups in the extent of tuberculosis or type of diabetes, but striking differences were seen in the results of treatment. Of diabetics treated for tuberculosis before 1950 one-quarter died from this disease within 7 years of the onset. There were no deaths among the patients receiving antibacterial drugs, and the diabetes was much easier to control in this group than in those patients treated before 1950. At the end of a 5-year period of observation it was found that 11 of the 21 deaths in the series were due to tuberculosis and occurred in patients who did not receive drug therapy. Of 46 surviving patients followed up for a minimum of 5 years the tuberculous process was arrested or quiescent in 29. Finally, it is pointed out that the mortality and the relapse rate in the present series were lower than in previous series; this was thought to be due to better control of the diabetes, less advanced tuberculosis initially, and the use of antibacterial drugs. *Joan Yell*

155. **Comparative Effects of Insulin and Orinase on Blood Levels of Pyruvate and *alpha*-Ketoglutarate in Normal Subjects**
A. R. HENNES, B. L. WAJCHENBERG, S. S. FAJANS, and J. W. CONN. *Metabolism* [*Metabolism*] **6**, 63–69, Jan., 1957. 2 figs., 11 refs.

In a further effort to elucidate the action of the sulphonylurea compounds in the metabolism of glucose the authors have investigated, at the University of Michigan Medical School, Ann Arbor, the blood levels of pyruvate and α-ketoglutarate during hypoglycaemia induced by insulin or "orinase" (tolbutamide) in 7 healthy subjects, 6 males and one female. The dosage was 0·05 unit of glucagon-free insulin per kg. body weight given intravenously and 1·0 g. or (in one case) 1·5 g. of sodium orinase intravenously or 6 g. of orinase orally (2 cases).

During the insulin-induced hypoglycaemia the blood pyruvate level rose in 7 out of 8 experiments, and showed a decrease during orinase-induced hypoglycaemia in 7 out of 9 experiments. The authors point out that these results preclude the induction of a rapid release of endogenous insulin as being the explanation of the mode of action of orinase. The blood levels of α-ketoglutarate followed no definite pattern during these experiments.
F. W. Chattaway

156. **Insulin Secretion following Carbutamide Injections in Normal Dogs**
G. POZZA, G. GALANSINO, and P. P. FOÀ. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **93**, 539–542, Dec., 1956. 2 figs., 21 refs.

The hypoglycaemic action of carbutamide, one of the orally active hypoglycaemic sulphonylureas, was investigated by means of 7 pancreatic–femoral and 5 mesenteric–femoral cross-circulation experiments on mongrel dogs of both sexes at the Chicago Medical School. The carbutamide was given intravenously in a dose of 50 mg. per kg. body weight. In 4 of the experiments, 2 pancreatic–femoral and 2 mesenteric–femoral, carbutamide had no effect on the blood glucose level of either the donor or the recipient animals. In the remaining 5 pancreatic–femoral cross-circulation experiments the substance caused a significant reduction (25 to 60%) in the blood glucose content of the donor dogs accompanied by a similar hypoglycaemia in the recipient dogs. In the mesenteric–femoral experiments the carbutamide caused hypoglycaemia in the donor animals only.

The absence of a hypoglycaemic effect in the recipient dogs of the mesenteric–femoral experiments made it unlikely that the hypoglycaemia observed in the recipient animals of the pancreatic–femoral series was due to carbutamide which had crossed the anastomoses. The blood carbutamide levels were found to be very similar in both types of recipient dogs. The results are therefore considered to be consistent with the hypothesis that carbutamide causes insulin secretion, although they do not allow differentiation to be made between the release of pre-formed insulin or an increase in true insulin secretion by the pancreas. *M. J. H. Smith*

157. **Effect of Aryl Sulfonylurea on the Plasma Disappearance of Labelled Insulin in Diabetics**
R. E. BOLINGER and H. J. GRADY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **233**, 182–185, Feb., 1957. 1 fig., 8 refs.

In order to test the hypothesis that the sulphonylurea drugs exert their hypoglycaemic action through an inhibition of the insulin-destroying enzyme insulinase the authors, working at the University of Kansas School of Medicine, Kansas City, have determined the rate of disappearance of insulin labelled with radioactive iodine from the plasma of 6 diabetic patients. In every case they found that " orinase " (tolbutamide) increased the rate of disappearance of radioactivity from the plasma. Extrapolation of the disappearance curves to zero time showed an increase in the theoretical concentration of insulin at that time in 4 of the patients (there was no change in one and a decrease in the other patient). This, the authors suggest, is compatible with the hypothesis that the sulphonylureas retard the rapid destruction of insulin by insulinase in the liver, thus making the insulin available to other tissues. The increased rate of disappearance is thought to be a reflection of the accelerated utilization of insulin in the tissues brought about by the drug. *Robert Mahler*

158. **Studies on a New Long-term Insulin: Zinc Methyl-albumin Insulin.** [In English]
O. SKENSVED. *Acta endocrinologica* [*Acta endocr. (Kbh.)*] **24**, 159–178, Feb., 1957. 10 figs., 14 refs.

The author describes the preparation of a new depot insulin, zinc–methyl-albumin insulin (Z.M.A.I.), in which human albumin, normally acid, is made alkaline by methylation and added to insulin together with zinc to give a preparation comparable in action to similar long-acting insulins, but not producing local reactions.

Clinical trials of this new " retard " preparation were then carried out on 22 adult diabetics, that is, all diabetics requiring insulin admitted to the Statshospital, Sønderborg, Denmark, " during a certain period ". The patients were first stabilized on ordinary insulin and then afterwards on Z.M.A.I., this usually requiring about 5 to 8 days, after which they were kept on a constant dose of Z.M.A.I. for the duration of the test period. All patients were ambulatory and were taking standard but unweighed diets. No difficulty was experienced in readjusting to the new insulin. The blood and urine sugar levels were frequently determined.

Control of the diabetes with Z.M.A.I. was " excellent " in 5 cases, " good " in 6, and " fair " in 4; in 5 there was insufficient evidence to judge, and in 2 control was definitely poor. Of 9 patients who had had excellent, good, or fair control with other types of insulin, 5 were better controlled with Z.M.A.I. and the other 4 were not worse. In the majority of cases the duration of action of Z.M.A.I. was between 21 and 24 hours, the minimum time being 18 hours. In all but one case the insulin was given in one injection at 8 a.m. The maximum effect occurred usually between 4 p.m. and 12 midnight, but in a few cases it was later, between 2 a.m. and 4 a.m. After breakfast the moderate rise in blood sugar returned to normal levels by 4 p.m.; the effect of meals taken after 11 a.m. was slight. No loss of consciousness occurred in any of the patients, and the incidence of side-reactions was the same as, or slightly less than, that with other similar long-acting insulins. No patient developed local allergic reactions to Z.M.A.I. while in hospital, but one did later; this patient, however, had previously reacted to insulin zinc suspension, and it is thought that the allergy was to zinc. The dosage required ranged from 12 to 80 units daily, the average being 38 units. In 8 cases a reduction and in 4 an increase in dosage was necessary on changing from other types of insulin. Of the 20 patients discharged taking Z.M.A.I. daily, the diabetes is still controlled after 2 years in 14. *A. Gordon Beckett*

159. **The Possible Influence of Hyperadrenocorticism on the Foetus of the Diabetic Woman**
J. W. FARQUHAR. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 483–501, Dec., 1956. 10 figs., bibliography.

In this paper from the University of Edinburgh and the Royal Edinburgh Hospital for Sick Children the author describes an attempt to determine whether the abnormalities observed in infants of diabetic mothers—for example, gigantism, hepatomegaly, and oedema—could be explained on the basis of excess excretion of adrenal steroids by the mother during pregnancy. The subjects were 17 infants born to diabetic mothers and 32 healthy infants, but the two groups were not strictly comparable because the healthy infants were born at full term whereas the others were delivered by Caesarean section at 36 weeks. One of the latter group died during the neonatal period. In all the infants the eosinophil count was determined at birth, 3 and 6 hours later, and daily thereafter. Urinary excretion of acid-stable formaldehydogenic steroids and 17-ketosteroids was determined in only 7 healthy infants and 14 infants born to diabetic mothers.

There was a spontaneous decrease in the number of circulating eosinophils during the first 6 hours of life in all except one of the abnormal infants, but in the healthy infants the eosinophil response varied. From the second to the tenth day the changes in the eosinophil count were extremely variable in both groups. No correlation was found between these changes and the blood sugar level in either group, nor between the blood count and the clinical condition of the abnormal infants.

The urinary excretion of acid-stable formaldehydogenic steroids in the first day of life was higher in the abnormal than in the healthy group, but by the third day it was similar in both groups. Excretion of 17-ketosteroids did not differ in the two groups, but volume of urine excreted daily was higher in the infants of diabetic mothers than in the healthy infants. There was no consistent correlation between the clinical condition of the infants and the steroid excretion.

[Although no positive conclusions are drawn by the author, this paper should be read by those interested in the subject for its full and clear discussion of the problems involved.] *T. D. Kellock*

The Rheumatic Diseases

160. **Some Points on the Pathogenesis and Diagnosis of Rheumatism.** (Некоторые данные о патогенезе ревматизма и его диагностике)
D. D. LEBEDEV and S. I. PETROV. *Советская Медицина [Sovetsk. Med.]* 3–6, No. 12, Dec., 1956. 3 figs.

In discussing the pathogenesis of rheumatism the authors tend to favour a combination of the theory of a specific allergy with that of a neurogenous element responsible for the complex of vegetative disturbances stated always to be associated with rheumatism, that is, sweating, instability of the pulse with a tendency to tachycardia, and a series of trophic changes, including atrophy of the small muscles and frequently also of the skin of the palm and sole, as well as frequent changes in tendon reflexes. Infection of the heart is particularly prone to occur in those with infection of the upper respiratory passages, and it is considered that particularly infections of the tonsils and throat are of special significance in relation to cardiac involvement, irritation in this region producing reflex cardiac dysfunction. Thus, Bogomolova by painful (needling) and thermal stimulation of the tonsils produced changes in the electrocardiogram (ECG) which were not produced by similar stimulation of skin areas. The present authors also produced ECG changes by intratonsillar injections of turpentine, which were repeated to simulate chronic tonsillitis; control animals receiving similar injections into the flank showing no comparable changes in the ECG. In dogs in which the left cerebral cortex had been removed irritation of the left tonsil produced greater changes in cardiac activity than did irritation of the right tonsil.

Cardiac involvement in rheumatism is therefore regarded as a complex of intoxication, allergy, and the results of functional disturbances and actual anatomical damage in nerve centres at various levels in the nervous system, from the cortex to the intramural nerves in the heart substance, this complex determining a reflex factor. The fact that removal of the focus in the throat does not always lead to regression of cardiac involvement may be explained partly by the occurrence of irreversible changes in the heart and in the nerves in its substance, and partly by continuing pathological irritation and reflexes from scar formation at the site of the resected tonsils or in intensively treated tonsils. *R. Crawford*

161. **The Rebound Phenomenon in Acute Rheumatic Fever**
K. S. HOLT. *Archives of Disease in Childhood [Arch. Dis. Childh.]* **31**, 444–451, Dec., 1956. 2 figs., 34 refs.

An attempt was made at Sheffield Children's Hospital to elucidate the mechanism of the "rebound" phenomenon, or transient relapse, sometimes seen following the cessation of treatment in patients with acute rheumatism. In all, 110 patients were studied and according to their treatment fell into five main groups: (1) 55 received "large" doses of salicylates (such as to maintain a serum salicylate level of 30 to 40 mg. per 100 ml.) and of these, 22 exhibited a rebound; (2) 17 received high doses of salicylates together with cortisone, and a rebound occurred in 7; (3) 13 children were treated with cortisone or ACTH (corticotrophin) alone, and a rebound was observed in 3 of these; (4) 8 patients received low doses of salicylates (20 to 30 grains (1·3 to 2 g.) daily) together with cortisone, with only one rebound; (5) 17 were treated with low doses of salicylates only, and again only one exhibited a rebound.

In 20 of the 34 cases in which a rebound occurred this consisted in elevation of the erythrocyte sedimentation rate only, but in 14 there were other clinical features. It is noted that rebounds were no more frequent after treatment with hormones than with salicylates in large doses, but were far fewer when small doses of salicylates were employed. A rebound was frequently associated with septic lesions (particularly in hormone-treated cases), the presence of beta-haemolytic streptococci in the throat, and a long illness before treatment was instituted. The incidence of the rebound was also high in adolescent girls. *C. Bruce Perry*

162. **Effect of Intramuscular Injection of Benzathine Penicillin G on Some Acute-phase Reactants**
R. C. HAAS, A. TARANTA, and H. F. WOOD. *New England Journal of Medicine [New Engl. J. Med.]* **256**, 152–155, Jan. 24, 1957. 1 fig., 7 refs.

A single intramuscular injection of 1,200,000 units of benzathine penicillin (N:N′-dibenzylethylene diamine dibenzylpenicillin) is known to provide prophylactic levels of penicillin for about one month and has been widely used for preventing recurrences of rheumatic fever as well as for the treatment of streptococcal pharyngitis. Most patients given such injections develop soreness and tenderness at the site of the injection, lasting for 1 to 3 days.

This study from Irvington House, Irvington-on-Hudson, and New York University is concerned with the clinical and serological effects of such injections in 40 children convalescent from rheumatic fever. C-reactive protein appeared in the serum in 22 cases (55%) 2 days after the injection and persisted for 1 to 5 days. About the same time 17 cases (42·5%) showed a raised erythrocyte sedimentation rate, and this continued somewhat longer. A rate of 20 mm. in one hour (Wintrobe) corrected for anaemia was considered to be the upper limit of normal, and levels up to 35 mm. an hour were recorded. In 5 cases (12·5%) there was a rise in temperature above 100·5° F. (38·05° C.) beginning during the first two days and lasting up to the third day. No fever or increase in erythrocyte sedimentation rate was seen following administration of 1,200,000 units of procaine benzylpenicillin to 11 children convalescent from rheumatic fever, although very small amounts of

C-reactive protein appeared in the serum after the injection in 2. There was no evidence of delayed sensitivity.

The authors have been unable to determine with certainty the nature of these reactions, but suggest they are due to benzathine penicillin as a compound and not to the penicillin as such, and should not be misinterpreted as evidence of a rebound or recurrence of rheumatic activity. *E. G. L. Bywaters*

CHRONIC RHEUMATISM

163. **Meprobamate (Miltown) in Rheumatic Diseases**
R. T. SMITH, I. F. HERMANN, K. M. KRON, and W. P. PEAK. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **163**, 535–538, Feb. 16, 1957. 2 figs., 4 refs.

Meprobamate, which is related chemically to mephenesin, is considered by the authors to have a muscle relaxant effect at least equal to its better known tranquillizing action. They have given the drug to 252 patients at the Benjamin Franklin Clinic, Philadelphia, suffering from diseases in which "fibrositic" symptoms predominated, and here report the results. Usually the dosage was 400 mg. in tablet form 3 or 4 times a day. The best results were obtained in patients with rheumatoid spondylitis or "fibrositis". Toxic effects were not serious; drowsiness, which was much the most common, was overcome or disappeared in the majority of patients when the dose was reduced. The only other side-effect which occurred with any frequency was slowing of the action of the bowel. The mild soporific effect was sometimes useful for sedation in agitated, tense, or nervous patients.

Similar symptoms were seen in some rheumatic patients taking "delta-steroids", and the authors therefore tried a combination of prednisolone and meprobamate in two strengths in capsule form—1 mg. of prednisolone with 200 mg. of meprobamate and 2 mg. of prednisolone with the same amount of meprobamate—which made it possible to provide 6 to 16 mg. of prednisolone daily without overdosage of the muscle relaxant. With these capsules treatment was simple and the desired results were more easily achieved. [No details are given.]

The authors conclude that meprobamate is one of the "best drugs presently available" for the relief of muscle spasm without loss of strength or function.

B. E. W. Mace

164. **Diagnosis, Treatment and Prevention of Chronic Hypercortisonism in Patients with Rheumatoid Arthritis**
C. H. SLOCUMB, H. F. POLLEY, L. E. WARD, and P. S. HENCH. *Annals of Internal Medicine* [*Ann. intern. Med.*] **46**, 86–101, Jan., 1957. 3 figs., 34 refs.

The great pharmacological potency of the steroid hormones has been abundantly demonstrated since their introduction in 1949 for the treatment of rheumatoid arthritis and other disorders. The problems associated with their employment to the best advantage and greatest safety have not yet, however, been completely solved, more especially when they are used for long-term treatment, as is the rational tendency of their modern use.

The authors discuss in this paper what they refer to as "the calculated acceptable risk" of "hypercortisonism" embodied in the decision to embark upon the long-term treatment of patients with any of these hormones. They discuss the clinical signs and symptoms of this condition and the need for slow and gradual reduction in the dosage of exogenous hormones. They stress the difficulties associated with this procedure, and outline the technique they have adopted. They emphasize the difference between the therapeutic effect achieved by optimally tolerated doses of cortisone and other steroid hormones, note the effects of chronic mild hormonal overdosage in patients with rheumatoid arthritis, and comment on certain special dangers associated with the latter. *W. S. C. Copeman*

165. **The Latex Fixation Test. I. Application to the Serologic Diagnosis of Rheumatoid Arthritis. II. Results in Rheumatoid Arthritis**
J. M. SINGER and C. M. PLOTZ. *American Journal of Medicine* [*Amer. J. Med.*] **21**, 888–892 and 893–896, Dec., 1956. 1 fig., 15 refs.

The Rose–Waaler diagnostic test for rheumatoid arthritis depends on the ability of the serum of rheumatoid arthritic patients to agglutinate particles (sheep erythrocytes) coated with globulin (rabbit anti-sheep-cell antibody). The authors, in the first of these papers from the Mount Sinai Hospital, New York, report experiments in which they showed that suspensions of polyvinyl toluene latex particles coated with commercial human gamma globulin show a similar specific agglutination reaction with arthritic sera. (Polysterene latex can also be used.) They describe the preparation and standardization of the latex suspension, and also the results in preliminary tests of minor variations in the methodology in respect of the *p*H, the order of addition of the reagents, the amount of gamma globulin used, the temperature, and the addition of electrolytes to the system. The method finally adopted is described. [The original paper must be consulted for details.] The test result is considered positive when agglutination is observed with a serum dilution of 1 in 20 or more. In clinical trials results compared well with other established techniques. The advantages of the test are that (1) it can be completed in a few hours, and (2) the reagents used are more susceptible to standardization.

In the second paper the results are reported of the use of the latex fixation technique to test 1,380 sera, 150 of which were from confirmed cases of rheumatoid arthritis. The number of cases and percentage positivity in each clinical group were as follows: 150 cases of rheumatoid arthritis, 71%; 120 of osteo- and other types of arthritis, 2%; 250 of rheumatic fever and rheumatic heart disease, 1·6%; 80 cases of diseases [unspecified] with hyperglobulinaemia, 5%; 20 of lupus erythematosus, 5%; 560 of non-arthritic disease, 3%; and sera from 200 normal subjects, 1%. The results are compared with those of the Rose differential sheep-cell agglutination test and the Heller test in rheumatoid

arthritis and various other conditions. Results for the latex fixation test were either positive or negative, whereas those for the sheep-cell agglutination tests were recorded as positive, negative, or doubtful. When the tests were compared on a basis of *negative* results the findings were as follows: latex test, 28·7% in rheumatoid arthritis and 97·5% in other diseases; the Rose test, 32 and 96·5% respectively; and the Heller test, 26 and 96·5% respectively. Serum from some individual patients might give a positive result in one test and a negative result in another test.

[This test is simpler than other specific tests for rheumatoid arthritis and promises to be as reliable.]

Allan St. J. Dixon

166. **The Fibrositic Nodule Experimentally Provoked in Ankylosing Spondylitis.** (Il nodulo fibrositico sperimentalmente provocato nella spondilite anchilosante) A. Gospodinoff and V. Baccarini. *Riforma medica* [*Rif. med.*] **71**, 8–12, Jan. 5, 1957. 4 figs., 25 refs.

Experiments were carried out at the Institute of Rheumatology of the University of Rome on 2 patients suffering from ankylosing spondylitis and 2 healthy control subjects of the same age and build. In each case an ethyl chloride spray was applied for 5 seconds to a limited area of skin over the flexed elbow on 2 or 3 successive days. While the healthy subjects showed nothing but transient hyperaemia, the patients with ankylosing spondylitis each developed a small nodule under the skin at the site of stimulation which was tender on pressure and, in one case, acted as a " trigger-point " for pain radiating down the forearm. Biopsy of the subcutaneous tissue containing the nodule showed histological changes deemed to be typical of fibrositis.

L. Michaelis

COLLAGEN DISEASES

167. **Studies of the Blood Chemistry in Collagen Disease.** (Ricerche sull'ematochimica delle malattie del collageno) L. Francalancia. *Rivista di clinica pediatrica* [*Riv. Clin. pediat.*] **58**, 285–318, Sept., 1956 [received Feb., 1957]. 13 figs., bibliography.

From the Paediatric Clinic of the University of Florence the author presents the results of various biochemical investigations of the blood in 3 cases of dermatomyositis, 2 of progressive myositis ossificans, and one of scleroderma, the biochemical methods used being briefly indicated. In 2 cases repeat tests were carried out after 30 to 50 days. Brief case histories are given, together with the dosage of cortisone and ACTH employed in 2 of the cases of dermatomyositis. The results are presented in tables, and electrophoretograms are reproduced.

The total plasma protein level was usually at first within normal limits and decreased slightly under treatment. The albumin fraction, which was relatively decreased but in absolute figures was almost normal, increased considerably during treatment in 2 of the cases of dermatomyositis. Plasma α_1 globulins showed wide variation both in relative and absolute values, but were never below the mean normal value. An increase in some cases was directly proportional to the severity of the illness or its progressive character, and the value usually decreased following hormone therapy. In 2 cases of dermatomyositis, one of myositis ossificans, and one of scleroderma the absolute value for α_2 globulin was increased, but all percentage values were in the vicinity of normal. The β-globulin values were generally normal, except in the case of scleroderma, but the γ-globulin levels were considerably increased in all the patients. The author favours Marmont's view that a primary noxious influence produces a change in the mesenchymal nucleoproteins, transforming them into endo-antigens, which in turn provoke antibody formation with a corresponding increase in the γ-globulin fraction.

The plasma lipoprotein content was normal in all cases, as also were the total lipid, cholesterol, and lipid phosphorus levels. In 2 cases of dermatomyositis there was, however, a marked increase in the lipid fractions during treatment, and a less pronounced increase occurred in a case treated with prednisone, followed in all 3 cases by an increase in the β-globulin value. The plasma mucoprotein, total non-glucosamine polysaccharide, and glucoprotein levels were increased, especially in 2 cases of dermatomyositis and in the 2 cases of myositis ossificans, in proportion to the severity and the progress of the disease. The ratio of total polysaccharides to total proteins was increased in all cases in parallel with the polysaccharide increase but independently of the levels of the other protein fractions. The literature is extensively reviewed.

F. Hillman

168. **Gastrointestinal Manifestations of Systemic Lupus Erythematosus**

C. H. Brown, E. K. Shirey, and J. R. Haserick. *Gastroenterology* [*Gastroenterology*] **31**, 649–664, Dec., 1956. 5 figs., 10 refs.

Some evidence of gastro-intestinal involvement was found in 32 out of 87 patients with proved systemic lupus erythematosus. In 25 of these the symptoms were of minor importance and responded rapidly to treatment. In the remaining 7, however, symptoms were severe; these 7 cases are described in detail in the present paper.

The symptoms were shown to be due to ileus in 5 patients, involving the stomach, duodenum, or jejunum. In 3 patients with duodenal ileus the radiological appearances were similar to those seen in the superior mesenteric artery syndrome. Radiographs in one patient with acute abdominal symptoms on admission revealed a perforated ulcer on the lesser curvature of the stomach, possibly a result of steroid therapy. The authors state that the treatment of ileus in such cases as these should be conservative, although surgical drainage was carried out in one case. Factors possibly responsible for ileus were collagen deposits in the submucosa, vascular changes associated with the primary disease, and autonomic involvement.

The remaining 2 patients in the authors' series had both lupus erythematosus and ulcerative colitis, and the many features common to both conditions are described.

J. N. Harris-Jones

Neurology and Neurosurgery

169. **An Electromyographic Study of Induced and Spontaneous Muscle Cramps**
F. H. NORRIS, E. L. GASTEIGER, and P. O. CHATFIELD. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **9**, 139–147, Feb., 1957. 6 figs., 36 refs.

The authors have utilized the electromyogram (EMG) to study spontaneous and induced muscle cramps (defined as " localized, involuntary, sustained, and painful contractions of skeletal muscles ") in normal individuals and in patients suffering from neurological disease of which cramps were a symptom. Recordings were made from microelectrodes, each of which had a recording surface area of approximately 100 sq. μ; these were inserted into the muscle through a hypodermic needle and were found to record discrete motor-unit potential activity much more satisfactorily than the larger concentric type of electrode. Of 121 college students, 115 had experienced spontaneous cramps at least once and 16% of these had experienced attacks during the night. It was found that cramp could very easily be induced by means of a maximal voluntary contraction when the muscle concerned was in a shortened position; the cramp could then be relieved by stretching the muscle. The rectus femoris and gastrocnemius were the most satisfactory muscles for these experiments, and as many as 5 or 6 microelectrodes could be inserted into either of these muscles at any one time. It was found that the muscle action potentials recorded during cramps took the form of normal motor-unit activity and did not resemble those seen following denervation or in disease of the muscle itself. The amount of pain associated with an attack of cramp was proportional to the amount of motor-unit activity which was recorded. The fact that the induction of reflex activity in the muscle concerned could sometimes abolish and sometimes produce a cramp, as well as the normal motor-unit activity accompanying it, indicated that this phenomenon was of central origin. The authors suggest that cramps may be due to a hyperexcitable state in the spinal cord, which may occur under physiological conditions but may be exaggerated in those neurological diseases of which cramps are a prominent symptom. *John N. Walton*

170. **Permanent Relief of Tic Douloureux by Gasserian Injection of Hot Water**
R. JAEGER. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Neurol. Psychiat.*] **77**, 1–7, Jan., 1957. 8 figs., 7 refs.

The author, from Jefferson Medical College and Hospital and Wills Eye Hospital, Philadelphia, describes a method of injecting hot water into the Gasserian ganglion under radiographic control and light anaesthesia for the relief of pain in tic douloureux, and discusses the results obtained in 100 cases. In 5 cases treated in the early stages of development of the method there was immediate recurrence of pain, which was relieved by subsequent sensory root section. In the last 70 patients treated there was only one failure, and a further injection in this case was later successful. Complications were few; the muscles of mastication on the injected side were weakened or paralysed in every case, but within 4 months there was complete return of power. Temporary diplopia lasting up to 5 months occurred in 5 patients, herpes was seen in a few—as occurs also after operation or injection of alcohol—and 2 suffered a mild meningeal reaction attributed to activation of intracranial herpes virus. Adequate analgesia over the affected area was obtained with this method; but complete facial analgesia was not necessary for the relief of pain. Corneal sensation thus remained intact and there were no visual disturbances.

The advantages claimed for this method are: (1) avoidance of major craniotomy in patients who are often old and otherwise unfit, and (2) the absence of risk of facial paralysis and of serious eye complications. The method is not recommended for use by those not fully conversant with intracranial anatomy. *J. B. Stanton*

171. **A New Congenital Non-progressive Myopathy**
G. M. SHY and K. R. MAGEE. *Brain* [*Brain*] **79**, 610–621, 1956. 11 figs., 10 refs.

From the National Institute of Neurological Diseases and Blindness, Bethesda, Maryland, the authors describe a myopathy affecting one female and 4 male members of a family in the course of 3 generations. The disease appeared to be congenital or to start within the first months of life, and in the early stages there was hypotonia and delay in walking. There was proximal muscle weakness in the legs and to a slight degree in the arms, but no change in the tendon reflexes. The chief histological abnormality on muscle biopsy was in the anatomical arrangement and histochemical characteristics of aberrant fibrillary bundles found in the centre of almost every muscle fibre.

The authors state that the disorder appeared to be non-progressive. *J. W. Aldren Turner*

172. **Itch Sensation and Recovery of Sensation in Spinal Cord Injuries**
A. J. ARIEFF, S. W. PYZIK, and E. L. TIGAY. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Neurol. Psychiat.*] **77**, 156–158, Feb., 1957. 8 refs.

At the Veterans Administration Hospital, Hines, Illinois, examinations were performed with itch powder containing the proteolytic enzyme mucunain on 14 quadriplegic and 4 crural paraplegic patients recovering from spinal cord injury. The areas selected for testing all showed recovery of sensation for pain, touch, or temperature.

In 27 skin areas of hypoalgesia or of decreased or absent sensation to pin-prick, but with good recovery to touch, no itch response was elicited, whereas in 16 areas of the skin in which a pin-prick was sharply felt the itch sensation was present. No itch sensation was produced by electric current applied to an area showing sharp pin-prick sensation, although the burning sensation experienced was described as painful. In one case, in spite of the presence of subjective pain, no pain was produced by pin-prick and no itch response was obtained. It is concluded that the sensation of itching is dependent on preservation of the sensation of pain.

G. de M. Rudolf

173. **Studies in Headache. Bulbar Conjunctival Ischemia and Muscle Contraction Headache**

A. M. OSTFELD, D. J. REIS, and H. G. WOLFF. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Neurol. Psychiat.*] **77**, 113–119, Feb., 1957. 4 figs., 8 refs.

The authors describe a series of investigations carried out at New York Hospital–Cornell Medical Center, New York, to determine the relationship, if any, between bulbar conjunctival ischaemia, muscle-contraction headache, and headache of the type occurring in migraine.

The first investigation consisted in the examination of 8 healthy, normotensive, male medical students 6 and 2 days before, on the day of, and 2 days after sitting a final examination in physiology—a "life situation" thought likely to cause some stress. In 7 of the 8 subjects a progressive increase in bulbar conjunctival ischaemia developed as the examination approached, which was followed by a decrease after the examination. In association with the ischaemia, feelings of tension, accompanied by rigidity, increase of foot and hand movements, rapidity of speech, and impatience with the eye examination were noted; there was no apparent correlation between the degree of conjunctival ischaemia and level of blood pressure. Increased sensitivity occurred to topical "levarterenol" (L-noradrenaline) given at *p*H 7·2 in isotonic phosphate buffer solution. The 8th subject in this group showed neither change in mood or behaviour nor conjunctival changes.

The remaining 8 experiments were undertaken in an attempt to clarify the mechanism of muscle-contraction headache. This usually bilateral type of headache is steady and non-throbbing, with a sensation of deep aching or pressing, and is unassociated with scotomata, nausea, vomiting, or a family history of such attacks. It may last for minutes or months and is usually located in the neck or occiput, but may be in the frontal, parietal, or temporal areas. Of 11 persons examined on 30 occasions before, during, and after such headache, increased sensitivity to noradrenaline and conjunctival ischaemia were found on 12 occasions during 14 attacks, these signs passing off as the headache diminished. To 50 of the patients on 12 occasions infusion of a 0·008% solution of noradrenaline bitartrate in 5% dextrose was given intravenously. Increase of the headache with vasoconstriction occurred while the agent was being given. Ergotamine tartrate in doses of 0·25 to 0·5 mg. increased the severity of the headache in 3 of 5 subjects. Inhalation of amyl nitrite was given to 5 subjects on 6 occasions; in all, slight conjunctival dilatation occurred and the headache decreased in 5 instances for up to 3 minutes. Hexamethonium bromide (25 mg. in 500 ml. of 5% dextrose in water) given intravenously had no effect on the ischaemia or the headache on 2 occasions in 2 subjects.

In one subject who had undergone left stellate ganglionectomy and right cervical sympathectomy, conjunctival ischaemia and increased sensitivity to noradrenaline occurred during 2 headaches. Oral administration of 100 mg. of cortisone produced conjunctival ischaemia from one to 4 hours later, but no headache occurred on 13 occasions in 3 subjects. Intravenous infusion of noradrenaline in 4 subjects during headache-free periods at a rate sufficient to produce ischaemia of the same degree as that occurring during headache did not induce headache. Intravenous phentolamine hydrochloride (10 mg.) was given on 3 occasions to 3 subjects. Decrease in headache and in ischaemia occurred 10 minutes later.

The conclusion is drawn that increases in the level of circulating catechol amines during states of anxiety and tension may initiate or intensify ischaemia about the head and so be related to muscle-contraction headache.

G. de M. Rudolf

CEREBRAL TRAUMA

174. **Medical Aspects of Boxing, Particularly from a Neurological Standpoint**

M. CRITCHLEY. *British Medical Journal* [*Brit. med. J.*] **1**, 357–362, Feb. 16, 1957. 33 refs.

The principal ill effects ascribed to boxing, with particular reference to neuropsychiatric deterioration, are discussed. The types of amnesia associated with boxing are: (1) retrograde amnesia, immediately preceding the spell of unconsciousness due to a "knock-out" blow; (2) a more lengthy period of permanent retrograde amnesia; and (3) anterograde amnesia. The author has had experience of 69 cases of chronic neurological disease in boxers, the majority being cases of "chronic progressive traumatic encephalopathy" ("punch-drunkenness") —that is, the gradual physical and mental deterioration which is the direct accumulated result of a boxing career. In only a few instances was there legitimate doubt about the possibility of some coincidental and non-related nervous or mental disease. There was a correlation between the degree of craniofacial marking and the intensity of the syndrome. As a rule, gradual evolution of mental and physical anomalies marks the insidious onset of the encephalopathy. Mental symptoms include the slow development of a fatuous or euphoric dementia with emotional lability and little insight. Speech and thought become progressively slower and memory deteriorates considerably. There may be swings of mood, intense irritability, and sometimes truculence, leading to uninhibited violent behaviour. Simple fatuous cheerfulness is, however, the commonest prevailing mood, although sometimes there is depression with a paranoid colouring.

The neurologist may encounter almost any combination of pyramidal extrapyramidal, and cerebellar signs:

tremor and dysarthria are two of the commonest signs. Types of punch-drunkenness in which pallidal and striatal defects are conspicuous appear to have been more frequent since the war. Here a mask-like face, slurred monotonous speech, extrapyramidal rigidity, infrequency and slowness of movement, and tremors of the arms and head constitute a syndrome superficially resembling a postencephalitic Parkinsonian state. The subject may admit to few disabilities; he may, however, complain of persistent dull headache, postural dizziness, deafness, poor vision, intolerance towards alcohol, unsteady gait, and shakiness.

The author states that the interval between the start of a boxing career and the onset of traumatic encephalopathy is usually a matter of years; in 21 naval patients the average was 16 years with a range of 6 to 40 years. Once established, the condition is progressive, even though the boxer retires. The electroencephalogram (EEG) reveals a non-specific type of disordered cortical rhythm, indicative merely of an atrophic process. The author summarizes his experience of the EEG in these cases as follows: (1) minor non-specific EEG anomalies are common in experienced boxers; (2) such anomalies are commoner and often more intense in cases of traumatic encephalopathy; (3) the EEG is a less sensitive index of the condition than is the clinical evidence; and (4) a return to normal in the EEG cannot be regarded as *restitutio ad integrum*, whether physiological, anatomical, or clinical. *John C. Kenna*

175. **Further Observations on the Medical Aspects of Amateur Boxing**
J. L. BLONSTEIN and E. CLARKE. *British Medical Journal* [*Brit. med. J.*] **1**, 362–364, Feb. 16, 1957. 29 refs.

The authors review the boxing injuries, especially those to the head, sustained in the 3,000 contests, involving about 5,000 boxers, of the London Amateur Boxing Association between October, 1955, and April, 1956. Under the medical welfare scheme instituted two years ago all contestants suffering concussion or lengthy periods of amnesia are rested for at least one month. From these, 29 who were more severely concussed were selected for special study. In all 29 instances a careful neurological examination was carried out soon after the injury, and an electroencephalogram (EEG) was recorded within 2 weeks of the knock-out in 7 cases and within 3 to 4 weeks in 22. No abnormalities of the central nervous system were detected in any of the 29 subjects and the EEG was normal. The authors give brief details of 3 cases which illustrate some of the varieties of memory loss encountered, for example, amnesia occurring without an obvious knock-out. In 3 of the remaining cases there was retrograde amnesia of up to one hour and in 7 the post-traumatic amnesia lasted from half an hour to 3 hours; the maximum period of unconsciousness, however, was half an hour. During the period covered by this investigation there were no skull fractures among the boxers, and injuries elsewhere in the body were few. One subject had a spontaneous pneumothorax, another a fractured fibula, and there were 11 cases of fractured metacarpal in the series, but none of the contestants had fracture of the nose or suffered serious eye injury.

The authors discuss medical control of amateur boxing at length. It is stated that deleterious cerebral changes may occur after an interval, but little evidence has been found in support of this. Much more information on boxing amnesia is required, and they suggest that assessment of the total traumatic amnesia may be more important than the neurological examination or the EEG in detecting the first signs of deleterious effects of boxing upon the brain. *John C. Kenna*

CEREBRAL VASCULAR DISORDERS

176. **Practical Drug Treatment of Migraine Headache**
J. G. OATMAN. *Antibiotic Medicine and Clinical Therapy* [*Antibiot. Med.*] **3**, 439–445, Dec., 1956. 7 refs.

The comparative efficacy of methyl*iso*octenylamine (" octin ") and ergot alkaloids in the treatment of migraine is discussed in this paper from the Veterans Administration Hospital and the University of Pittsburgh School of Medicine, Pittsburgh. Of 23 unselected consecutive patients suffering from migraine, 6 received preparations of ergot, 9 methyl*iso*octenylamine, and 8 a combination of both. Treatment with methyl*iso*octenylamine was initiated with a subcutaneous injection of 50 mg. of the drug. Blood pressure was then recorded frequently to detect the onset of hypertension—a possible side-effect which, it is pointed out, may have a sympathomimetic action.

The author found that it was possible to obtain a satisfactory response with either ergot or methyl*iso*octenylamine, there being little difference between the two preparations in this respect. Methyl*iso*octenylamine, however, was preferable to ergot preparations for prolonged treatment, because its constrictive action on vessels was not cumulative. *Fergus R. Ferguson*

177. **Retinal Arterial Pressure Studies Associated with Cervical Carotid Artery Occlusion in the Treatment of Cerebral Aneurysms**
R. W. RAND. *Bulletin of the Los Angeles Neurological Society* [*Bull. Los Angeles neurol. Soc.*] **21**, 175–187, Dec., 1956. 3 figs., 19 refs.

The object of the investigation described herein was to study the bilateral retinal arterial pressure and the internal carotid arterial pressure before, during, and after occlusion of the carotid artery, and thus to establish the role which ophthalmodynamometry could play during ligation of the vessel. An attempt was also made to assess the late effects of carotid artery occlusion on retinal arterial pressure.

For measuring the retinal arterial pressure the author used a Bailliart ophthalmodynamometer, pressure being applied to the anaesthetized eyeball during an ophthalmoscopic examination. The pressure reading obtained on the instrument when the first maximal expansile arterial pulsation at the papilla was noted represented the diastolic pressure, and the reading taken at the point of cessation of expansile arterial pulsation represented the

systolic pressure. Actual pressures could then be calculated in mm. Hg if the ocular tension was known.

A detailed study of 3 cases of subarachnoid haemorrhage due to a ruptured intracranial aneurysm showed that changes in retinal arterial pressure closely parallel pressure changes in the internal carotid artery, as determined by direct measurements. At the follow-up examination a significant difference in pressure between the two eyes was maintained in 2 cases, although it was less than at first. In the third case this difference was minimal and the author attributes this to re-establishment of collateral circulation from the ipsilateral external carotid artery. *Marcel Malden*

EPILEPSY

178. **The Surgical Treatment of Non-tumoral Temporal Epilepsy.** (Traitement chirurgical de l'épilepsie temporale non tumorale)
J. E. PAILLAS and P. PRUVOT. *Presse médicale* [*Presse méd.*] **65**, 197–199, Feb. 2, 1957. 23 refs.

This paper presents the results of follow-up for periods up to 7 years of 45 patients treated at the Hôpital de la Timone, Marseilles, by temporal lobectomy for temporal-lobe epilepsy not due to tumour. The operation was one of wide temporal lobectomy extending back to the vein of Labbé, usually with removal of the uncus, Ammon's horn, amygdaloid nucleus, and insula. At follow-up 13 patients were free from seizures, 3 having been so for more than 5 years and 6 for more than 3 years, while in a further 11 cases the frequency of fits had been reduced by 75% or more. The remaining 21 cases in which seizures were not reduced to this extent were regarded as unbenefited. Personality disorders before operation had been prominent in 37 patients (7 were in institutions on this account) and of these, 18 were benefited, the improvement being greater in those with aggressive outbursts rather than in those with paranoid disorders. In 19 cases the postoperative electroencephalogram (EEG) showed disappearance of the focal spike discharges and return to a normal pattern, but these changes were not closely correlated with the postoperative cessation or continuation of seizures. The few sequelae which could be attributed to the operation were superior quadrantanopia in 3 cases, dysphasia in one, and some impairment of intellect in the 2 patients subjected to bilateral temporal lobectomy. Audiometric investigation of the cochlear and vestibular functions one to 4 years after operation showed slight defect on the side contralateral to the lobectomy, or bilateral defect in some cases subjected to left-sided operation, with abolition of induced vertigo and variable anomalies of optokinetic nystagmus.

The results are analysed in detail and indications for the operation are discussed. The authors conclude that the greatest chance of success is in those cases in which there is a circumscribed unilateral EEG focus from a lesion of dystocic or traumatic aetiology, and with radiological evidence of anatomical abnormality of the temporal lobe. They believe that progress in the field of temporal lobectomy for the relief of epilepsy will result less from improvement in operative technique than from careful selection of cases, and in particular the elimination of those cases of centroencephalic epilepsy which simulate temporal-lobe epilepsy but which cannot, by their nature, be benefited by lobectomy. *J. B. Stanton*

179. **The Action of Anticonvulsant Drugs Tested by Electrical Stimulation of the Cortex, Diencephalon and Rhinencephalon in the Unanesthetized Rabbit**
H. GANGLOFF and M. MONNIER. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **9**, 43–58, Feb., 1957. 6 figs., bibliography.

The authors, working at the Laboratory of Applied Neurophysiology, Geneva, have employed a stereotactic method of stimulating electrically the cerebral cortex, the diencephalon (thalamus), and the rhinencephalon of rabbits in the investigation of the action of certain anticonvulsant drugs. By means of experiments upon 10 unanaesthetized animals they first defined the results normally to be expected from such stimulation, paying particular attention to electrographic recordings of the electrically-induced after-discharge. The effects of the anticonvulsant drugs upon these responses were then studied in groups of 5 rabbits. It was found that diphenylhydantoin decreased selectively the excitability of the diencephalon, while phenurone reduced the excitability of the diencephalon and the cortex and modified the rhinencephalic after-discharge pattern. Troxidone proved to be a powerful depressant of cortical excitability, and also reduced the responses from the diencephalon and rhinencephalon, though this effect was less striking; phenobarbitone, on the other hand, while reducing the activity induced in the diencephalon and rhinencephalon, actually increased cortical excitability.

[The authors make a number of assumptions about the effects of these drugs in clinical epilepsy which are not entirely justified by their results; however, these experiments, which cannot be described adequately in an abstract, are important as they confirm that the various anticonvulsant drugs may have selective effects on different areas of the brain.] *John N. Walton*

180. **Variations in Arterial Pressure Provoked by Epileptic Attacks.** (Les variations de la pression artérielle provoquées par les crises d'épilepsie)
G. MORIN and J. CORRIOL. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **9**, 59–82, Feb., 1957. 15 figs., bibliography.

The authors, working in the Physiological Laboratory of the Faculty of Medicine of Marseilles, have studied the effects upon the arterial blood pressure of electrically-induced epileptic seizures in 125 conscious but curarized dogs of both sexes. They found that a major seizure produced marked hypertension, which began when the fit became generalized and ended simultaneously with the end of the clonic movements. The nature of the epileptogenic stimulus had no influence upon the production of hypertension, but selective stimulation of numerous brain areas, both deep and superficial, revealed that the epileptic discharge must affect the frontal pole for

hypertension to occur, although stimulation of the frontal pole alone was insufficient. It was also apparent that the hypertension developed only when the electrical discharge reached the "pressor area of the diencephalon". This diencephalic activation, and hence the hypertension, could be inhibited by doses of anaesthetics or chlorpromazine which were insufficient to influence the character of the seizure. It is concluded that the occurrence of hypertension accompanying an epileptic seizure is dependent upon the spread of the epileptic discharge to the hypothalamic region, and that the pressor effect is mediated by peripheral autonomic pathways, though there is also an increased secretion of adrenaline. *John N. Walton*

181. **Laughter in Epilepsy**
R. DRUCKMAN and D. CHAO. *Neurology* [*Neurology*] 7, 26–36, Jan., 1957. 16 refs.

This paper from the Methodist Hospital (Baylor University College of Medicine), Houston, Texas, describes 11 cases in which laughter was an epileptic manifestation. The laughter varied from a violent, prolonged attack lasting 2 minutes or so to giggling or merely grinning. An epileptic origin of the laughter was indicated by the lack of any external precipitant, by the nature of the laughter, by concomitant manifestations of epilepsy, and by response to anticonvulsant drugs. The clinical and electroencephalographic picture in these cases showed much variation, but in general indicated the possibility of an organic lesion of the brain as a cause. The clinical abnormalities included mental impairment, hemiparesis, hemiatrophy, and spasticity. No patient showed signs suggesting a large hypothalamic lesion, but the evidence that the hypothalamus may be involved in such cases, at least in part, is discussed.

[See also *Abstracts of World Medicine*, 1957, **21**, 422.]
J. MacD. Holmes

182. **Long-term Effects of Phensuximide ("Milontin")**
J. REY-BELLET and W. G. LENNOX. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Neurol. Psychiat.*] 77, 23–27, Jan., 1957. 1 fig., 6 refs.

The results of a long-term follow-up study at the Children's Medical Center, Boston, of 249 patients given phensuximide ("milontin") for epilepsy are reported. Preliminary results based on one to 3 years' treatment were published in 1955 (Davidson *et al.*, *New Engl. J. Med.* **253**, 173), and in the present paper these earlier results are compared with those obtained after a further 2 years' treatment. The patients were suffering from petit mal, grand mal, or focal seizures, the first of these predominating. The dosage of phensuximide ranged from 0·5 to 5·0 g. daily. The number of seizures experienced daily before and during treatment was recorded, and when there was a reduction of 90% or more the results were classified as "excellent", results showing a reduction of 50 to 90% as "good", and when the reduction was less than 50% they were classified as "poor". It was found that in 66% of patients suffering from petit mal with excellent initial control seizures were still well controlled 2 years later, and 25% of these had stopped treatment. Of those with grand mal or focal seizures and excellent initial control, 75% maintained that position after 2 years, 3% having stopped treatment. Of those with good control initially, 35% with grand mal or focal seizures and 24% with petit mal were included 2 years later in the group with excellent control; but in 12% of the patients with petit mal and 3% with grand mal or focal attacks control had deteriorated and they were included in the group showing poor control. Similar but less marked shifts were observed in the group in which initial control had been poor.

The authors state that in general early improvement correlated with continued improvement, but if initial improvement was less than 50% very little was to be gained by a longer trial. No serious side-effects of the drug were encountered. *J. B. Stanton*

MIDBRAIN

183. **Clinical Results and Follow-up Studies in a Personal Series of 300 Operations for Parkinsonism**
I. S. COOPER. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **4**, 1171–1181, Dec., 1956.

The author describes his results in the surgical treatment of Parkinsonism in two groups of cases: (1) 55 cases treated by occlusion of the anterior choroidal artery; and (2) 245 cases treated by chemopallidectomy.

Of the patients in Group 1, 75% were relieved of muscular rigidity and 65% of tremor, and in these cases there was a marked reduction in the degree of incapacity. It is stated that when the benefits of this form of treatment endure for 4 months they are likely to persist. The operative mortality in this group was 10% and the incidence of hemiplegia 8%.

Chemopallidectomy (instillation of alcohol into the globus pallidus) relieves the tremor and rigidity in 85% of cases, but during the subsequent week these disturbances re-appear in some measure. By leaving the cannula in position and performing further injections during the next 7 to 10 days these early recurrences can be prevented and in almost 80% of cases relief is maintained for 8 weeks after the operation. Altogether 70% of the author's patients in Group 2 showed relief at intervals ranging from 3 to 24 months after operation and without impairment of motor or sensory function. The mortality of chemopallidectomy was 2·8% and the incidence of hemiplegia 2%. Mental disturbance, confusion, hypersomnia, and negativism were frequent, but usually transient. Dysphasia occurred in 15% but was severe and persistent in only 2 cases. Increased autonomic disturbance—hyperhidrosis, hyperthermia, and hypersalivation—was never of long duration.

In reviewing the results as a whole the author states that the condition of patients who have undergone surgical treatment is invariably better than that of similar patients not so treated, which always deteriorates progressively, their disease never becoming spontaneously arrested. He considers that occlusion of the anterior choroidal artery should be reserved for younger patients

with a long history and severe disability, and might also be preferred in centres dealing with only the occasional case of Parkinsonism. Chemopallidectomy is simpler and safer, although for satisfactory results a careful study of the whole problem of Parkinsonism is essential. The author indicates that much remains to be discovered in connexion with this disease. *J. E. A. O'Connell*

184. **Chemopallidectomy for Dystonia Musculorum Deformans**

I. S. COOPER, N. POLOUKHINE, and T. I. HOEN. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] 4, 1208–1213, Dec., 1956. 3 figs., 3 refs.

Increasing experience of the surgical attack upon the globus pallidus and the afferent pathways in the treatment of the tremor and rigidity of Parkinsonism has suggested to the authors that other types of dyskinesia may be benefited by the procedure. The findings that dystonic deformities of the hands and feet in Parkinsonian patients might be removed by this treatment and that choreiform and athetoid movements in some cases of post-encephalitic Parkinsonism were diminished after operation led to a trial of the treatment in 20 children showing gross dystonia and dyskinesia, and in the present paper one of these cases is described in detail.

The patient, a girl aged 12 years, had developed progressive dystonia musculorum over a period of 4 years and had become completely incapacitated, requiring heavy sedation and continuous nursing attention. Catheters were passed into the globus pallidus on both sides and instillation of procaine abolished the involuntary movements without producing paralysis. Injections of 0·4 ml. of a solution of cellulose in 95% alcohol was then made—the catheters remaining *in situ*. There was immediate dramatic improvement and on the fourth postoperative day a further injection of 0·3 ml. of the solution was effected on each side and the catheters withdrawn. During the subsequent follow-up period of 2 months the patient progressed rapidly so that she was able to walk, run, cycle, and dance. Dystonic deformities disappeared and, apart from twitchings of the erectores spinae, no involuntary movements occurred. The authors consider that the globus pallidus forms part of the neuronal circuit concerned not only in tremor and rigidity, but also in the gross movements of chorea, athetosis, and dystonia musculorum deformans.

J. E. A. O'Connell

185. **Effects of Anterior Choroidal Artery Occlusion and of Chemopallidectomy on the Tremor and Rigidity of Parkinson's Disease: an Independent Appraisal**

L. DILLER, M. RIKLAN, and Z. LASZEWSKI. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] 4, 1246–1248, Dec., 1956. 5 refs.

The results of occlusion of the anterior choroidal artery in 16 patients and of chemopallidectomy in 96 patients with Parkinsonism were assessed clinically before, and again 3 to 6 weeks after operation at St. Barnabas Hospital, New York. The condition of each patient was independently assessed by at least 3 members of a team including surgeons, physicians, psychologists, a speech therapist, a nurse, and specialists in physical medicine and physiotherapy and a pooled rating thereby arrived at.

Of 16 patients treated by occlusion of the anterior choroidal artery, in 10 (63%) tremor and rigidity were improved, and in 6 (37%) they were unimproved (3 being worse than before operation). (" Improvement " implies anything from a slight reduction to complete disappearance of tremor and rigidity.) Of 59 patients treated by subtemporal chemopallidectomy, 42 (71%) were improved and 17 (29%) not benefited, 13% being worse. Of 37 patients treated by transfrontal chemopallidectomy, 34 (91%) were improved and 3 (9%) unimproved.

Of the whole group, about 40% showed increased ability to carry out the activities of daily life, some 25% showed an improvement in mental status, while 34% had deteriorated.

[Although the team of independent observers were agreed on the occurrence of some improvement in a high proportion of cases in the early weeks after the surgical treatment of Parkinson's disease, the analysis does not indicate its degree in individual cases or the value to the patients of the treatment described.]

J. E. A. O'Connell

186. **Follow-up Study of the Results of Anterior Choroidal Artery Occlusion and Subtemporal Chemopallidectomy in Parkinson's Disease: an Independent Appraisal**

L. DILLER, M. RIKLAN, and J. WOOD. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] 4, 1249–1257, Dec., 1956. 4 refs.

This paper from St. Barnabas Hospital, New York, reports the findings in 23 cases of Parkinsonism treated by occlusion of the anterior choroidal artery on follow-up 18 to 36 months after operation and in 29 cases treated by subtemporal chemopallidectomy after 9 to 13 months. The inquiry was conducted by postal questionary to which 85% of the patients responded, and was concerned with the motor and non-motor aspects of the disease as well as with the patients' opinion of the value of the procedure.

Of the motor disturbances, tremor was reduced or absent in 77% of both groups and was unchanged or worse in 23%; rigidity was lessened in 16 (69%) of the patients treated by arterial occlusion and in 18 (62%) of those treated by chemopallidectomy, being worse in 5 (22%) of the former group and 5 (17%) of the latter. Of those patients who were improved on discharge from hospital, deterioration in varying degree had occurred in 28%. The reduction in tremor and rigidity facilitated the performance of the activities of daily life in 12 (52%) of the former and 19 (65%) of the latter group, the patients' difficulties being increased in 5 (22%) and 6 (21%) respectively.

Of the disturbances classified as non-motor, facial expression was improved in 69% of patients treated by choroidal occlusion and 58% of those treated by chemopallidectomy, there being deterioration in this respect in 9% and 13% respectively. Oiliness of the skin was reduced in 34% of all patients and in 11% the skin was considered to be too dry. Nervousness was reduced

in 59%. Speech function deteriorated more often than it was improved after operation, and memory likewise was more often worse after operation than improved. Depression was lessened in rather more than one-third of the patients after surgery and increased in rather less than one-third. Fatiguability was reduced and an improvement in general health was recorded in about 50% of cases. From the point of view of employment, 25% of the patients who had not worked before the operation were able to do so after it, while 33% were able to resume household duties. As regards the patients' opinion of the operation, 41% were completely satisfied, 25% expressed qualified satisfaction, and 31% were disappointed.

[The observers here are led to the conclusion that both anterior choroidal arterial occlusion and chemopallidectomy benefit patients with Parkinson's disease. This study does not, however, reveal clearly the degree of this benefit.] *J. E. A. O'Connell*

DEMYELINATING DISEASES

187. **Observations on the Prevalence of Multiple Sclerosis in Northern Scotland**
J. M. SUTHERLAND. *Brain* [*Brain*] **79**, 635–654, 1956. 2 figs., 35 refs.

The author has surveyed the incidence of disseminated sclerosis in the seven most northerly counties of Scotland, the total population of which is about 231,000. The over-all incidence of the disease appeared to be about 5·5 "probable" cases per 10,000 people. The prevalence varied in different parts of the area: in Shetland and the Orkneys it reached the high figure of 11·8 per 10,000, whereas in the Western Isles (including Skye) it was 3·8 per 10,000. The author suggests that there may be a constitutional vulnerability to the disease in the predominantly Nordic population of Shetland and the Orkneys as compared with the more Celtic population of the Western Isles. The familial occurrence of the disease was also studied in the same area, and in about 11% of cases a relative was found who was apparently suffering from the same disease.

[This is a valuable survey comparable with that in Northern Ireland by Allison and Millar (*Ulster med. J.*, 1954, **23**, Suppl. 2; *Abstracts of World Medicine*, 1954, **16**, 410).] *J. W. Aldren Turner*

188. **Flicker Fusion Thresholds in Multiple Sclerosis**
O. A. PARSONS and P. N. MILLER. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Neurol. Psychiat.*] **77**, 134–139, Feb., 1957. 16 refs.

At Duke University School of Medicine, Durham, North Carolina, the flicker-fusion threshold was determined in 20 male patients with disseminated sclerosis, 20 male non-neurological patients serving as controls. Each subject was given 10 runs of flickering light (at 20 or 10 c.p.s.) in 5 ascending and 5 descending series, in steps of 0·5 cycle. After 30 seconds rest, 2 further tests of 10 runs each, separated by 30 seconds, were given. No smoking was allowed for at least 15 minutes before the test and no drugs known to alter the flicker-fusion threshold were given. Cases of severe psychiatric disturbance were excluded.

The flicker-fusion threshold mean value for the patients with disseminated sclerosis was 29·77 c.p.s. and for controls 40·23 c.p.s., this difference being statistically significant. Division of the patients into those showing pallor of the optic disk (9 cases) and those without such pallor (11 cases) gave means of 24·70 and 33·91 c.p.s., the difference between each figure and that of the controls being significant at least at the level of $P<\cdot01$. It is suggested that the lower flicker-fusion threshold thus demonstrated in patients with disseminated sclerosis may be of value in the diagnosis of this disease, since in 16 (including all those with pallor of the disk) of the 20 patients studied the threshold was below 37·1 c.p.s., that is, below the lowest threshold obtained in any of the controls. The authors believe that the lowered threshold is due to optic neuropathy accompanying retrobulbar neuritis. *G. de M. Rudolf*

189. **Observations on the Feeding of Fatty Acids from Cerebrosides to Patients with Disseminated Sclerosis**
R. L. NOBLE, K. K. CARROLL, and A. S. DOUGLAS. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **76**, 23–26, Jan. 1, 1957. 23 refs.

The authors point out that "cerebrosides are unique among classes of lipids in that they contain, apparently exclusively, extra long chain fatty acids with 24 or 26 rather than the usual 18 carbon atoms". It is suggested, therefore, that these acids "may have some specific functional role in the metabolism of the nervous system". As they are unlikely to occur in any quantity in food the body must be able to synthesize them, and since cerebrosides occur chiefly in the myelin of the central nervous system, a deficiency resulting from failure of the synthetic mechanism might be expected to be associated with some form of neurological disorder.

On this assumption they have treated patients with various neurological conditions with cerebroside preparations extracted from beef spinal cord, and in this paper from the University of Western Ontario they report their observations on 6 patients with disseminated sclerosis who were given this substance. The duration of treatment and follow-up varied from 7 to 17 months and although during the period of observation no spectacular improvement has been observed, none of the patients has experienced a major exacerbation. While no conclusions can yet be drawn, it is suggested that repetition and extension of these preliminary tests appear to be justified.

[One cannot help feeling that this paper would have been of far more value had there been a longer period of observation.] *N. S. Alcock*

190. **Blood Coagulation Studies and Serotonin Determinations in Serum and Cerebrospinal Fluid in Multiple Sclerosis.** [In English]
S. FELDMAN, G. IZAK, and D. NELKEN. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. neurol. scand.*] **32**, 37–49, 1957. 39 refs.

Psychiatry

191. **Natural History of Obsessional States. A Study of 150 Cases**

J. POLLITT. *British Medical Journal* [*Brit. med. J.*] 1, 194–198, Jan. 26, 1957. 5 figs., 11 refs.

The natural history of " pure " obsessional illness was studied in 150 patients (63 males and 87 females), 69 of whom had been in-patients at the Atkinson Morley Hospital (St. George's Hospital), London, and the remainder were seen in private practice. It proved possible to follow up 101 patients for periods of 3 months to 15 years. The mean age at which the first symptoms appeared was 21·58 years in females and 21·16 years in males; only 4 patients experienced the first symptom after the age of 45. In half the patients the disease ran an episodic course, with an average of two attacks before the patient was first seen. Most attacks lasted one year or less, and were often precipitated by stress, particularly sexual traumata. Of 82 patients followed up for one year or more, 55 were symptom-free and able to lead a normal life; of 45 followed up for 4 or more years, 29 were symptom-free and leading a normal life. Recovery, when it occurred, was seen more often in the early years of the illness than later; it was seen less frequently in cases of long duration. Recovery was gradual and seldom smooth, and treatment, with the possible exception of leucotomy (34 patients), was rarely followed by immediate and sustained recovery. Only one patient committed suicide (4 years after leucotomy); in another patient schizophrenia later developed.

The author compares these findings with those previously reported. He concludes that the prognosis in the obsessional state is much better than is usually thought to be the case and " the view that it has an inevitable gloomy outcome " is not supported by the evidence. *J. B. Stanton*

192. **Polyneuropathy as a Complication of Disulfiram Therapy of Alcoholism**

M. HAYMAN and P. A. WILKINS. *Quarterly Journal of Studies on Alcohol* [*Quart. J. Stud. Alcohol*] **17**, 601–607, Dec., 1956. 6 refs.

According to the authors polyneuropathy is a frequent complication of disulfiram therapy, and in this paper from the Compton Sanitarium and the Beverly–Compton Day Therapy Center, Beverly Hills, California, they describe 7 cases in which polyneuropathy developed during a course of treatment with this drug. Of the 7 patients (4 males and 3 females, aged 21 to 55 years) 6 were typical alcoholics, each with a long history, continuous or episodic, of consuming more than a pint (473 ml.) of whisky a day. The remaining patient, a woman, had a much more moderate record in which alcoholism played a relatively minor part. None had any previous history of polyneuropathy.

The dosage of disulfiram was 2 g., 1·5 g., 1 g., and thereafter 0·5 g. on successive days. Disulfiram–alcohol reactions with the equivalent of 8 to 15 ml. of absolute alcohol were evoked on the 5th and 8th days, then once a week for several weeks, then once a month, and finally every 2 months to the end of the year, except when polyneuropathy intervened. In 5 of the patients polyneuropathy developed gradually over periods varying from 4 to 9 months. All the patients were leading well ordered lives, taking a good diet and more than the minimum daily requirement of vitamins. However, the authors suggest that in 6 of the 7 cases polyneuropathy was due to inability of a disulfiram-intoxicated nervous system to make proper use of the vitamins. Polyneuropathy in the remaining case is attributed to an allergic reaction following the disulfiram–alcohol test. Treatment consisted in cessation of disulfiram and administration of polyvitamin preparations. The outcome in all cases was favourable. *R. J. Matthews*

193. **Serial Liver-function and Blood Studies in Patients Receiving Chlorpromazine**

R. DICKES, V. SCHENKER, and L. DEUTSCH. *New England Journal of Medicine* [*New Engl. J. Med.*] **256**, 1–7, Jan. 3, 1957. 4 figs., 10 refs.

The authors have studied the blood and hepatic function in 50 acutely disturbed psychotic patients of both sexes, the majority aged between 20 and 45 years, who were receiving chlorpromazine in doses ranging from 124 to 647 mg. daily for periods varying from 7 to 51 days. Liver function was assessed by the " bromsulphalein " retention test, the serum alkaline-phosphatase and total serum bilirubin levels, and the cephalin flocculation test. The blood count and haemoglobin value were determined concurrently, all tests being performed three times a week when possible.

Some disturbance of liver function was detected in 22 cases at the outset. In the remaining 28 patients liver function was normal at first and in 11 cases remained so throughout, but in the other 17 patients various abnormalities developed. Of the 22 patients with initial abnormalities, 11 showed further impairment of liver function in response to chlorpromazine, but there appeared to be no correlation between the severity of the impairment and the dose or route of administration (intramuscular or oral) of the drug. Treatment had to be stopped in 8 cases because of the toxic effects on hepatic function. The bromsulphalein retention test and changes in the serum alkaline-phosphatase level were the earliest indicators of liver dysfunction due to chlorpromazine. It appeared that patients with initial liver damage, provided it was minor in degree, were no more likely to develop liver impairment from chlorpromazine than those with normal liver function. Leucopenia, eosinophilia, and the presence of immature cells were often noted. Leucopenia occurring during treatment with chlorpromazine is considered to be a definite contra-indication to further therapy. *Norval Taylor*

Dermatology

194. **The Behaviour of Radioactive Sulphur after Its External Application to the Skin**
A. SCOTT. *British Journal of Dermatology* [*Brit. J. Derm.*] **69**, 39–49, Feb., 1957. 6 figs., 7 refs.

An investigation of the pattern of sulphur absorption through normal skin and the alterations in this pattern in the presence of a dermatosis is reported in this paper from St. Bartholomew's Hospital, London, the radioactive isotope of sulphur (^{35}S) being used and its distribution studied with Geiger counters and autoradiography. It was found that when a hydrous emulsifying ointment containing ^{35}S and stable sulphur was applied to a defined area of skin, sulphur readily penetrated the epidermis, without preference for appendages, and had disappeared from the epidermis within 24 hours. It appeared to follow an intercellular route. In seborrhoeic dermatitis and psoriasis the sulphur was held in the epidermis intracellularly and did not penetrate into the dermis; in 4 to 12 hours it had been disposed of by outward transfer. With appropriate treatment of the skin disease the pattern of disposal of sulphur returned to normal. In acne, disposal of the sulphur was similar to that in normal skin, except that there was greater concentration in follicles.

The author suggests that this pattern of sulphur disposal is related to the keratogenous activities of epidermis.
John T. Ingram

195. **Current Treatment of Tuberculosis of the Skin. Results in 369 Cases Treated between 1941 and 1956.** (Les traitements actuels des tuberculoses de la peau; d'après une statistique de 369 cas traités de 1941 à 1956)
C. HURIEZ and P. H. PELCE. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **33**, 571–580, Feb. 14, 1957. 33 figs.

Practising in Lille and neighbourhood, where the incidence of cutaneous tuberculosis is higher than in other parts of France, the authors have treated 369 patients suffering from this disorder in the 15-year period 1941–56.

Of patients with lupus vulgaris [the number treated is not given], one-third were cured by administration of large doses of vitamin D_2 (calciferol) and remained so for many years. The addition of antibiotics (streptomycin, with or without PAS) in alternating courses with calciferol resulted in the cure of 55% of such patients. Isoniazid was also used with success. In a small proportion of resistant cases additional treatment by means of perfusions of PAS or ACTH (corticotrophin) was required. Of patients with warty tuberculosis treated with calciferol, only 16% were cured, but of 9 treated with isoniazid and streptomycin followed by long courses of calciferol, all were cured. In cases of scrofuloderma isoniazid was not so effective, even when injected locally, but treatment with antibiotics and corticotrophin in such cases resulted in a cure rate of 80%. The authors also consider the treatment of tuberculides and of sarcoidosis. The theory and methods of treatment of tuberculosis of the skin are discussed.

[In the absence of detailed data assessment of the results of treatment is difficult.] *S. T. Anning*

196. **The Outcome of Patients with Herpes Zoster**
J. M. DE MORAGAS and R. R. KIERLAND. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **75**, 193–196, Feb., 1957. 2 refs.

In an attempt to construct a picture of the natural course of disease in herpes zoster, a review was made at the Mayo Clinic of the records of 916 patients with this diagnosis (including post-herpetic neuralgia), all of whom had received standard treatment. The incidence of herpes zoster was greatest in the older age groups, while neuralgia increased in both severity and frequency in direct relation to age (16·7% under age 20, 91·3% over age 70). Generalization developed in 1% of cases and 4·2% of the total were associated with a lymphoma. Trigeminal involvement was present in 16·3%, and presented the greatest number of complications, including the loss of the eye. No one form of therapy proved effective in shortening or relieving the attack, and even such radical procedures as rhizotomy were relatively valueless.

Two therapeutic points are made: (1) that no form of therapy which helps only the young patient is of much value, since such cases are almost always mild in nature; and (2) that radical methods of treatment for the control of pain should be considered only as a last resort, since usually the neuralgia will improve spontaneously in time, while a high incidence of failures and of added complications is associated with the more drastic forms of therapy. *Allene Scott*

197. **Serodiagnosis with Antigens of *Treponema pallidum* in Lupus Erythematosus**
C. R. REIN, L. CHARGIN, and L. C. KELCEC. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **75**, 230–235, Feb., 1957. 17 refs.

Following upon the work of Moore on the biological false positive reaction for syphilis in systemic lupus erythematosus (*Ann. intern. Med.*, 1952, **37**, 1156, and *J. chron. Dis.*, 1955, **1**, 297; *Abstracts of World Medicine*, 1953, **14**, 110, and 1955, **18**, 408) a series of 79 cases of known clinical lupus erythematosus were examined at the University and Mount Sinai Hospitals, New York. A battery of standard serological tests for syphilis (S.T.S.) was employed as well as the recently introduced immune adherence, complement-fixation, and in some cases immobilization tests employing the specific antigens of *Treponema pallidum* (T.P. tests). In 35 cases the patient's serum gave positive results with the S.T.S.,

while only in 3 were positive reactions obtained with the T.P. tests. Two of the latter patients had known syphilis, while the third result was unexplained. The authors underline the usefulness of the T.P. tests in distinguishing false positive reactors, and suggest that the T.P. complement-fixation test, because of the ease and cheapness of its performance, is the most suitable for wider use.

[The article includes a good summary of previous publications on this subject.] *Allene Scott*

198. **Subcorneal Pustular Dermatosis**
I. B. SNEDDON and D. S. WILKINSON. *British Journal of Dermatology* [*Brit. J. Derm.*] **68**, 385–394, Dec., 1956. 4 figs., 17 refs.

The authors summarize 3 previous cases and describe 3 new cases of a chronic or relapsing vesicopustular eruption of an unusual pattern affecting mainly (5 of the 6 cases) middle-aged women (average age at onset 54·8 years). They regard the condition as an entity distinct from dermatitis herpetiformis, the pemphigus group, and also from impetigo herpetiformis. The axillae, groins, abdomen, and flexor aspects of the proximal parts of the limbs are particularly affected, the hands, feet, face, and mucous surfaces being entirely spared. The blisters tend to form circinate and gyrate patterns with an actively spreading edge, and individual lesions are indistinguishable from bullous impetigo.

Cultures from intact pustules or vesicles were either sterile or grew *Staphylococcus albus* or *Staph. aureus*, but in no case was *Candida albicans* found, although specifically looked for. The constant histological feature was a subcorneal blister filled with polymorphonuclear leucocytes, but no change in the epidermal cells, such as acantholysis, was apparent. An infective basis for the eruption was excluded by the clinical features, the very protracted course, and the complete failure to respond to local and systemic antibiotics, particularly nystatin. Diaminodiphenylsulphone (dapsone) was successful in controlling the eruption in 4 of the 6 cases. *E. W. Prosser Thomas*

199. **Generalized Pustular Bacterid. Its Relationship to the Pustular Dermatosis of Sneddon and Wilkinson**
F. F. HELLIER. *British Journal of Dermatology* [*Brit. J. Derm.*] **68**, 395–399, Dec., 1956. 3 figs., 2 refs.

The case is described from the General Infirmary at Leeds of a man aged 54 who was seen with "pustular bacterid" of the palms and soles of 6 years' duration. He then also developed vesicopustules on the trunk which formed circinate and guttate erythematous patches. Cultures of swabs were sterile; examination of skin biopsy specimens showed only vesicular spaces filled with polymorphonuclear leucocytes lying just under the horny layer. There was no acantholysis. The eruption cleared after administration of sulphapyridine, but the drug had to be withdrawn because of intolerance. There was, however, an excellent response to dapsone given in doses of 25 mg. twice daily. The author therefore considers that the lesions described above and those described by Sneddon and Wilkinson [see Abstract 198] represent the same disorder, the uncommon site in the present case accounting for their somewhat different appearance. *E. W. Prosser Thomas*

200. **Lethal Bullous Form of Congenital Ichthyosiform Erythrodermia.** (L'érythrodermie ichtyosiforme congénitale bulleuse létale)
S. LAPIÈRE. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph. (Paris)*] **84**, 5–21, Jan.–Feb., 1957. 6 figs., 29 refs.

In this paper from the University of Liège congenital ichthyosis is discussed and a comparison drawn between the lethal type of congenital ichthyosiform erythrodermia (harlequin foetus) and a lethal type, not before described, in which bullae are the striking feature. Cases illustrative of each type are presented (including a description, with photographs, of the clinical and histological features) and the differential diagnosis from epidermolysis bullosa, the epidermodysplasia of Lutz and Lewandowsky, Darier's disease, and Ritter's epidemic pemphigus is discussed. *S. T. Anning*

201. **A Follow-up Study of Hemangiomas of the Skin Treated and Untreated**
W. FALK and D. LEVY. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **93**, 165–172, Feb., 1957. 22 refs.

The condition of the "strawberry" type of vascular naevus when first observed in 60 children at Rambain Government Hospital, Haifa, was compared with its condition after a lapse of 5 to 8 years. When first seen the children were between one month and 4½ years of age, 52 being under 2 years. Since some had more than one lesion a total of 72 naevi in all were considered. In 14 cases the lesions had been treated with radium, but all the others (58) were treated conservatively. Of the latter, 51 (87·7%) were classified as showing a "perfect" result, that is, the naevus had disappeared completely with no scarring, whereas of the 14 treated with radium, only one (7·14%) showed a perfect result. Of the other conservatively treated lesions, only 4 (7·2% of the total) were classified as "failures" (persistence of the naevus) or as "poor" (with a retracted scar), whereas of those treated with radium, 8 (57·14%) were so classified. Both these differences are statistically highly significant [though the numbers are small]. Consideration of the results according to site gave similar results. Thus 5 naevi of the face were treated conservatively and all completely disappeared without scarring, compared with 2 fair and 2 poor results (some degree of scarring) in the 4 naevi of the face treated with radium. Similarly, a perfect result was obtained in all 12 naevi of the scalp and neck treated conservatively, compared with only one out of the 6 at the same site treated with radium.

Nevertheless, the authors in discussing their results continue to advocate active treatment in skilled hands for naevi that threaten to give severe cosmetic blemish, and also for those causing functional impairment with haemorrhage or ulceration. Conservative treatment is obviously better in all other types. They deprecate the use of carbon dioxide "snow". *E. H. Johnson*

Paediatrics

202. **Abnormalities in Meconium of the Foetus and Newborn**
J. L. EMERY. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **32**, 17–21, Feb., 1957. 8 figs., 30 refs.

After discussing the composition of meconium the author describes ano-rectal plugs, meconium plugs higher in the intestine, meconium bodies, and colonic stercoral ulceration in the neonatal period. He considers that all these abnormalities arise from local functional abnormalities related to the state of " suspended animation " of the foetal intestine in late pregnancy.

The ano-rectal plugs may be due to immaturity of the rectal expulsive mechanism and the others to abnormalities of water balance in the affected areas of the intestine. *Wilfrid Gaisford*

203. **Thyroid Disorders in the Newborn**
I. D. RILEY and G. SCLARE. *British Medical Journal* [*Brit. med. J.*] **1**, 979–980, April 27, 1957. 4 figs., 32 refs.

204. **The Phosphate Partition of the Erythrocytes of Normal Newborn Infants and of Infants with Hemolytic Disease**
T. J. GREENWALT and V. E. AYERS. *Journal of Clinical Investigation* [*J. clin. Invest.*] **35**, 1404–1411, Dec., 1956. 45 refs.

In a study undertaken at the Blood Center, Milwaukee, Wisconsin, to determine whether the action of specific antibodies produces any alteration of the phosphate fractions in foetal erythrocytes, the authors compared the phosphate partitioning in erythrocytes of cord blood from 16 healthy newborn infants with that in adult erythrocytes (fresh and after storage at 4° C.), and also with that in cord blood from 10 infants with anti-D haemolytic disease. The phosphate in erythrocytes is present as (1) inorganic phosphate, (2) labile phosphate, mainly from adenosine triphosphate, released by 7-minute hydrolysis, (3) phosphate hydrolysable after 100 minutes, split from adenosine monophosphate and hexose phosphates, and (4) non-hydrolysable phosphate largely derived from 2:3-disphosphoglycerate.

There was a significantly higher level of inorganic phosphorus in fresh cord blood than in erythrocytes of adults after storage for 3 weeks at 4° C. or in fresh adult erythrocytes. The easily hydrolysed and non-hydrolysed fractions decreased less and the " 100-minute " fraction increased more than in adult erythrocytes after storage. The easily hydrolysed phosphate fraction of fresh cord erythrocytes was significantly smaller than in cells from adults and infants with haemolytic disease. In the latter the inorganic phosphate concentration rose and the 7- and 100-minute hydrolysis fractions decreased at a significantly greater rate than in normal cord erythrocytes during storage. All the changes in phosphate partition produced by storage or incubation could be reversed by the addition of adenosine *in vitro* to the erythrocytes of normal infants and of infants with haemolytic disease. However, the addition of anti-D serum had no significant effect on phosphate partitioning. *M. Sandler*

CLINICAL PAEDIATRICS

205. **Clinical Application of " Royal Jelly " in Paediatrics.** (Applicazioni cliniche della " gelée royale " in campo pediatrico)
P. PROSPERI and F. RAGAZZINI. *Rivista di clinica pediatrica* [*Riv. Clin. pediat.*] **58**, 319–332, Sept., 1956 [received Feb., 1957]. 4 figs.

At the Paediatric Clinic of the University of Florence the authors have used " royal jelly ", the food of the queen-bee, in the treatment of 42 infants and children who failed to thrive, of whom 8 were premature infants. To 2 of the premature infants the jelly was given on the 3rd day of life and to the other 6 at the age of 14 to 37 days and continued for 9 to 40 days after other therapeutic attempts to produce a weight gain had failed. Of the remaining 34 patients, 15 were males and 19 females ranging in age from 22 days to 7½ years. Various different preparations of the jelly were used, it being given in the form of a watery alcoholic solution containing " 8 to 10 mg. per phial ", as a lyophylized product (50 mg. per phial), or as a 100-mg. capsule of the stabilized fresh substance.

One of the premature infants suffering from severe sepsis died in spite of treatment, and another similar patient had begun to improve when he had to be discharged from hospital. A third premature infant with intracranial haemorrhage and a weight curve stationary for 17 days gained 240 g. in 10 days, while the remaining 5 premature infants showed distinct and marked weight gain in response to the treatment. The 34 older patients, some of whom had additional illnesses, all gained weight under treatment, 12 of them more than 1 kg. and one as much as 2·5 kg. in one month. In a few cases the gain in weight was very small; generally speaking, those with endocrine or irreversible metabolic or cerebral disturbances responded poorly.

Royal jelly produces an increase in appetite, and treatment begins to take effect after 20 days. Growth may cease on interruption of treatment, but starts again on reinstitution of therapy. The haemoglobin level and erythrocyte count both improve during treatment, and serum protein levels usually become normal. The mode of action of the jelly is not yet clear; it is a concentrated protein gel containing some 31% of protein, with a *p*H of 3·5 to 4·5 and a high content of amino-acids, sugars, enzymes, and vitamins, especially those of the B group.

[Unfortunately the dosage is not clearly indicated, and although frequent reference to the literature is made in the text the relevant bibliographical details are not given.] *F. Hillman*

206. **Effect of Penicillins V and G on Carriers of Various Groups of Streptococci in a Children's Home**
P. F. WEHRLE, H. A. FELDMAN, and K. KURODA. *Pediatrics* [*Pediatrics*] **19**, 208–216, Feb., 1957. 11 refs.

The authors report from the State University of New York that following an outbreak of scarlet fever in a children's home at Syracuse, New York, a comparison was made between the effects of oral "penicillin V" (phenoxymethyl penicillin) and oral benzylpenicillin in the prophylactic treatment of streptococcal carriers. The former preparation, given in a daily dosage of 400,000 units divided in two doses for 10 days, successfully eliminated Group-A streptococci from the nasopharynx of carriers; a smaller dosage than this was not so effective. Similar results were obtained with oral benzylpenicillin in single or divided doses totalling 500,000 units daily for 10 days. The authors also observed a high incidence of infection with streptococci of Group G without, however, any associated clinical disease. *Winston Turner*

207. ***Salmonella* Osteomyelitis Complicating Sickle Cell Disease**
J. G. HUGHES and D. S. CARROLL. *Pediatrics* [*Pediatrics*] 19, 184–191, Feb., 1957. 4 figs., 5 refs.

A review of the literature has shown that there have been only 9 recorded cases of osteomyelitis due to *Salmonella* infection occurring in children with sickle-cell disease, but this paper reports 4 such cases all from the John Gaston Children's Hospital, Memphis, Tennessee. The clinical histories of these patients and the response to treatment with appropriate antibiotics are described. The authors state that this type of osteomyelitis complicating sickle-cell disease usually involves several bones. The radiographic appearances are characteristic, showing laminated periosteal proliferation with patchy destruction of bone and marked cortical fissuring. The authors conclude that children with sickle-cell disease have a special tendency to develop osteomyelitis and that *Salmonella* is often the infecting organism. *Winston Turner*

208. **Phenylalanine-restricted Diets in the Treatment of Phenylketonuria**
J. D. BLAINEY and R. GULLIFORD. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 452–466, Dec., 1956. 7 figs., 22 refs.

Previous reports of the beneficial effect of a diet low in phenylalanine content on the growth, development, and mentality of phenylketonuric mentally defective children have been somewhat inconclusive. In the study here reported from the University of Birmingham, 6 such children were treated for up to 3 years on diets providing 110 Cal. per kg. body weight per day, of which 70% was in the form of carbohydrate, and restricting the amount of phenylalanine to 15 mg. per kg. per day; the main source of nitrogen in the diet was casein hydrolysate from which the amino-acids tyrosine, cystine, and tryptophan had been largely removed. Each month the children were weighed and clinically examined, blood was taken for determination of haemoglobin and phenylalanine levels, and the urine was tested for phenylpyruvic acid and examined by paper chromatography for the presence of phenylalanine and other amino-acids; the urine was also examined for tryptophan derivatives, as these have been suggested as being responsible for the mental defect in these children. Four different tests of mental capacity were carried out by the same person; the Griffiths method of testing was not available until much of the work had already been completed. Full detailed case reports are given of all 6 children [but these require individual examination].

With strict adherence to the diet apparent biochemical normality was obtained, and with it normal growth and physical development for long periods. Long-term mental improvement was, however, limited, but this might well have been due to the infrequency of adequate biochemical control or because of the practical difficulties of strict adherence to such a diet in the patient's home. In one child strictly dieted in hospital there was considerable improvement, his initial mental age of less than 6 months rising to one of 12 months during a 15-month period. In 2 other children treatment was not started till they were over 5 years of age and in them there was little mental improvement. From these and other studies it seems clear that the age at which treatment is started is very important, particularly as children learn so much in the first 2 or 3 years of life. In spite of the limited increase in mental capacity improvement was noted in the patients' locomotion, manner and bearing, in awareness of surroundings, and in manipulation of objects.

[The environment would also appear to play a considerable part in the progress of these children.]
David Morris

209. **The Effect of Oral Lactose on Faecal Flora and *p*H in Infantile Gastro-enteritis**
B. ZILBERG. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 523–526, Dec., 1956. 2 figs., 13 refs.

It has been suggested that the growth in the intestinal tract of strains of *Escherichia coli* causing diarrhoea in infants may be influenced by certain environmental factors. The purpose of the study here reported from the Children's Hospital, Birmingham, was to investigate the effect of various oral doses of lactose on the faecal *p*H and lactobacillary flora of babies suffering from gastro-enteritis.

On admission to hospital 32 infants with signs of gastro-enteritis were allocated alternately to the "lactose group" or to a control group; before the start of therapy a specimen of faeces for bacteriological examination was obtained from each child. The earlier cases were given a 5% solution of lactose in saline, but this concentration was subsequently increased to 10% and later to 20%. The results suggested that administration of high doses

of lactose (20%) to infants suffering from gastro-enteritis may produce a temporary reduction in faecal *p*H and also a temporary increase in faecal lactobacilli. Lactose as used in this trial did not appear to exert any significant suppressive effect on the excretion of specific serological types of *Esch. coli.* *J. M. Smellie*

210. **Salivary Electrolytes in Fibrocystic Disease of the Pancreas**
W. H. JOHNSTON. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 477–480, Dec., 1956. 3 figs., 12 refs.

By means of a small metallic device made to adhere to the buccal mucous membrane around the orifice of Stenson's duct pure parotid saliva was obtained from 31 children with proven fibrocystic disease of the pancreas at the Hospital for Sick Children, Great Ormond Street, London, 63 other children with various diseases serving as controls. The parotid secretions thus obtained were analysed for their sodium, chloride, and potassium content.

The results showed a considerable difference between the mean concentration of salivary sodium in the fibrocystic group and that in the controls, but individual values were widely scattered. The difference in salivary chloride concentration was less and the overlap more marked, while there was practically no difference between the two groups in regard to salivary potassium concentration. It was noted that the rate of flow of parotid secretion was more rapid in the patients with fibrocystic disease and the concentrations of sodium and chloride tended to increase in both groups as the rate of flow increased. It is concluded, however, that the overlap between the values obtained in the two groups was too great to make the estimation of sodium and chloride in parotid secretion of much practical value in the diagnosis of fibrocystic disease of the pancreas. *J. M. Smellie*

211. **Proteolytic Activity of the Pancreas. Transient Depression in Infancy**
J. G. BATE and U. JAMES. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 506–511, Dec., 1956. 5 figs., 20 refs.

At the Princess Louise Hospital for Children (St. Mary's Hospital), London, the proteolytic activity of the duodenal fluid and the amino-acid absorption curve were determined in a study of three groups of children suffering from chronic gastro-enteritis, acute gastro-enteritis, and malnutrition respectively; the methods are described. In 10 cases of chronic gastro-enteritis thus examined initial investigations pointed to a diagnosis of fibrocystic disease of the pancreas and pancreatin was administered. Re-investigation after periods varying from 2 months to 2 years, during which time the patients continued to receive pancreatin, revealed normal duodenal trypsin levels, and satisfactory progress was maintained when pancreatin was discontinued. Of the 9 infants suffering from acute gastro-enteritis, all showed a moderately low amino-acid absorption curve within one week of the cessation of the diarrhoea, but the duodenal trypsin content was normal in 6. In 2 children who failed to progress satisfactorily administration of pancreatin led to recovery and when this was complete the amino-acid absorption curve had risen to normal. These absorption curves were also abnormal in the 8 infants with signs of malnutrition, the marasmus in these cases being considered to be due to under-feeding after failure of breast-feeding. Normal curves and clinical improvement were obtained after 3 weeks of oral pancreatin in one child and in a second without administration of pancreatin. [The results in the other 6 cases not mentioned.]

These findings suggest that fibrocystic disease of the pancreas should never be diagnosed on the findings of one series of investigations, even when duodenal trypsin is absent and the amino-acid curve flat. Reassessment should always be made several weeks or months later, when nutrition has been improved by diet and, if necessay, administration of pancreatin. *J. M. Smellie*

212. **Alkaline Resistant (Fetal) Hemoglobin in Hypochromic Microcytic Anemias of Infancy and Childhood**
I. LAI-FONG SZETO, G. ASROW, and H. N. SANFORD. *Journal of Pediatrics* [*J. Pediat.*] **50**, 49–51, Jan., 1957. 1 fig., 4 refs.

The foetal haemoglobin content of the blood of 102 normal infants aged 4 months to 7 years was determined by the authors at the University of Illinois College of Medicine, Chicago. These infants were judged to be free from haematological disorders, the blood picture and the electrophoretic pattern of the haemoglobin being normal. It was found that foetal haemoglobin values ranged up to 4% at the beginning of the second year of life, and that the upper limit of the normal range did not fall below 2% until the second half of the third year. When the foetal haemoglobin content of the blood of 18 anaemic infants varying in age from 4 to 28 months was determined it was found that the values fell well within the normal range. The cause of the anaemia was malnutrition involving an iron-deficient diet plus an infection in 12 cases and prematurity in 6.

H. Lehmann

213. **Renal Function in Children with Leukemia. A Clinical and Pathological Study**
E. F. GILBERT, E. C. RICE, and P. A. LECHAUX. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **93**, 150–156, Feb., 1957. 25 refs.

Simple renal function studies were performed by the authors at the Children's Hospital of the District of Columbia on 35 children who were suffering from confirmed leukaemia, 28 of them having acute and one chronic lymphatic leukaemia, and 3 having acute and 3 chronic myeloid leukaemia.

It was found that the concentrating ability of the kidneys following deprivation of fluid was unimpaired, urea clearance was normal in all 4 children in whom it was tested, and albumin was not present in the urine in a concentration greater than 50 mg. per 100 ml. unless there was haematuria, which did occur in 8 children in the terminal phase of the disease. The blood urea level, measured by a spectrophotometric method

using glycerol urease, was elevated in 13 patients above the normal value of 16 mg. per 100 ml. In 13 of the 14 children examined at necropsy leukaemic infiltration of the kidneys, particularly of the cortex, was found and the kidneys were slightly enlarged and showed haemorrhagic areas. As the authors point out, such gross parenchymal changes seem surprising in view of the relatively slight impairment of renal function in these patients during life. *T. B. Begg*

214. **The Day and Night Output of Urine in Enuresis**
D. Vulliamy. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 439–443, Dec., 1956. 3 figs., 9 refs.

It has been suggested that nocturnal polyuria is a contributory cause of enuresis, and the author of this paper has attempted to confirm this by studying the diurnal and nocturnal urinary output in 22 enuretic children (including only 2 females) and 24 non-enuretic children, aged 5 to 12 years. Both groups received a standardized diet and fluid intake for the 5 days and nights of the investigation, this period being preceded by 2 days of regulated fluid intake and diet. The output of sodium and potassium was also estimated over the 5-day period.

No significant difference was observed between the two groups in the average day:night ratio of urinary output; moreover urinary excretion of sodium and potassium was the same in both groups. However, bladder capacity, as judged by the maximum volume of urine passed in one act of micturition during the period of study, was relatively smaller in the children with enuresis than in controls. An interesting incidental observation was the high relative nocturnal polyuria in 2 children with steatorrhoea which was not always accompanied by enuresis.
David Morris

215. **Anuria Ascribed to Acute Tubular Necrosis in Infancy and Early Childhood**
I. J. Carré and J. R. Squire. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 512–522, Dec., 1956. 4 figs., 32 refs.

The authors describe 3 cases of acute renal failure, ascribed to acute tubular necrosis, which were encountered at the Children's Hospital, Birmingham, during 1952 and 1953. The first case occurred in a girl aged 5 years who had pneumonia (treated with penicillin and aureomycin) and also vomiting and dehydration. After 12 days of anuria or oliguria she made a good recovery, but a superadded urinary infection with *Candida albicans* left her with a contracted bladder and frequency of micturition. The second patient was a 7-month-old boy who had 10 days of anuria or oliguria following the treatment with sulphonamides of an upper respiratory infection; he also had a superadded urinary infection due to *Pseudomonas pyocyanea*. In the third case an 8-month-old girl who had been treated with penicillin for otitis media developed vascular collapse and a sensitivity rash, and subsequently had 9 days of anuria or oliguria. The 3 patients were treated conservatively, receiving by tube a fat and sugar emulsion giving 75 to 100 Cal. per kg. body weight daily, with careful maintenance of fluid and electrolyte balance. Cation-exchange resin in the hydrogen cycle was used to combat hyperpotassaemia in one case. All 3 children developed normocytic anaemia at a rapid rate during the period of renal failure.

During diuresis the patients showed evidence of impaired tubular function, manifested by glycosuria, amino-aciduria, poor concentration of urea, impaired conservation of sodium, potassium and chloride, and impaired production of ammonia. Approximate estimates of the chloride, sodium, and potassium balances were made and it appeared that cellular potassium had exchanged for cellular sodium during the anuria, this process being reversed during diuresis. Such ionic transfers, as well as intestinal and urinary loss of water and electrolytes, have to be taken into consideration in the management of fluid balance. During the first day or two of the early diuretic phase, or until the serum potassium level has fallen to normal, the authors combat urinary fluid loss by giving a continuous gastric drip of a solution containing 0·15 g. of sodium chloride and 0·2 g. of sodium bicarbonate per 100 ml. Subsequently a stock solution is used which contains 0·35 g. of potassium chloride and 0·45 g. of sodium bicarbonate per 100 ml. The 2 patients who were catheterized developed urinary infections, and this procedure is therefore to be deprecated in such cases. When seen at follow-up 2 to 3 years after the acute illness none of the patients was hypertensive and the renal clearance of endogenous creatinine was found to be within normal limits. *K. G. Lowe*

216. **Urolithiasis in Childhood**
N. A. A. Myers. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **32**, 48–57, Feb., 1957. 7 figs., 4 refs.

The author comments on the decreasing incidence of stones in the urinary tract in childhood, and on the relatively higher incidence of phosphatic stones and more frequent involvement of the upper urinary tract than formerly. On the basis of a study of 85 cases admitted to the Hospital for Sick Children, Great Ormond Street, London, during the past 20 years he classifies the causes as: (1) underlying congenital abnormalities (25 cases); (2) metabolic disorders (9 cases); (3) a miscellaneous group of recognizable causes such as neurogenic bladder, foreign body, and nephrocalcinosis (5 cases); and (4) unknown—by far the largest group, with 46 cases, among which was only one case of vesical calculus.

Boys were more often affected than girls (5:2) and the peak incidence was in the age group 0–4 years. Infection occurred in 60 of the 85 cases and *Proteus vulgaris* was the predominant organism in 60% of these. The stones were phosphatic in 50 cases and pure cystine in 5. The outstanding symptom was haematuria.

It is recommended that in cases of suspected urolithiasis in children the investigations should be threefold: (1) radiological—all the stones in this series were radio-opaque; (2) metabolic, particularly to exclude cystinuria and oxaluria; and (3) bacteriological, the presence of *Proteus* being suggestive of an underlying urolithiasis.
Wilfrid Gaisford

Medical Genetics

217. **Recent Advances in the Knowledge of Hereditary Ocular Diseases.** (Neues aus der Erbpathologie des Auges)
H. RIEGER. *Klinische Monatsblätter für Augenheilkunde* [*Klin. Mbl. Augenheilk.*] **128**, 513–526, 1956.

The main subjects discussed in this review of hereditary ocular diseases, presented from the Municipal Hospital, Linz, Austria, are refractive errors, idiopathic retinal detachment, and retinoblastoma. The author states that there is evidence that astigmatism is hereditary, both in degree and axis, in most cases being due to a dominant hereditary character. The theory that corneal refraction and axial length are completely independent is criticized. Myopia is more likely to be due to a defect in retinal growth, and both myopia and hypermetropia are considered to be probably the result of ectodermal malformations. Idiopathic retinal detachment has commonly been thought to be a complication of high myopia, and Lindner and many others considered that there was no evidence to demonstrate a purely hereditary factor in such detachments; however, histological investigations have shown that there may be a hereditary defect in the glial supporting tissues in this condition and a number of case histories are given to support the view that idiopathic retinal detachment has a specific hereditary basis. It is pointed out that in assessing the hereditary background of retinoblastoma the great number of isolated cases must be considered. In the remainder of the paper the author discusses many particular examples of congenital ocular disease.

[Although there are numerous references to the literature throughout the text, no bibliography is appended to the paper.] *B. A. Bembridge*

218. **Heredity and Rheumatic Fever. Some Later Information about Data Collected in 1950–51**
A. C. STEVENSON and E. A. CHEESEMAN. *Annals of Human Genetics* [*Ann. hum. Genet.*] **21**, 139–144, Nov., 1956. 10 refs.

In a previous paper (*Ann. Eugen.* (*Camb.*), 1953, **17**, 177; *Abstracts of World Medicine*, 1953, **14**, 342) the authors estimated the familial incidence of rheumatic fever in 462 Belfast families ascertained through an affected child and first visited in 1950–1. They now present further information obtained on revisiting the same families in 1955. Of the original 462 families, 19 were not traced. In the remainder 28 sibs of the original propositi previously unaffected have now developed rheumatic fever. The revised figures for the percentage of sibs affected are now: with neither parent affected 6·4 (±0·7), with father affected 14·3 (±3·4), with mother affected 9·9 (±2·4). The corresponding figures for the risk to sibs, calculated by Haldane's q^s method, are 11·2% (±1·1), 22·1% (±4·9), and 16·6% (±3·6) respectively. In 51 families ascertained through an affected mother, one of the original 156 children has since had a first attack of rheumatic fever, making 10 in all.

The authors note that any attempt to estimate proportions of sibs affected in sibships whose members have not reached early adult life is bound to result in an underestimate of the true familial incidence of the disease. *C. O. Carter*

219. **Hereditary Factors in Reactive Mesenchymal Diseases (" Collagen Diseases "). III. Common Genetic Predisposition to Rheumatic Fever and Rheumatoid Arthritis.** (Sulla eredopatologia delle mesenchimopatie reattive (cosidette malattie del collageno). III. Sulla comune predisposizione genetica al reumatismo acuto primario e al reumatismo cronico primario)
G. G. NERI SERNERI and V. BARTOLI. *Acta geneticae medicae et Gemellologiae* [*Acta Genet. med.* (*Roma*)] **6**, 25–44, Jan., 1957. 30 refs.

In this paper the authors examine the question whether there is a common hereditary predisposition to rheumatic fever and rheumatoid arthritis. The index cases were drawn from a consecutive series of 602 recorded at the Institute of Pathology of the University of Florence between 1940 and 1955. It was possible to examine the families of 479 of these patients, of whom 287 had had rheumatic fever and 192 rheumatoid arthritis. All these families lived in or near Florence. The examination included the first-degree relatives and, where possible, the second-degree relatives of the index cases. A similar examination was made concurrently of the families of 300 control subjects—patients with acute or chronic infective disorders and psychoneuroses.

The authors found that among the relatives of persons with a history of rheumatic fever there was not only a higher incidence of rheumatic fever than among the relatives of the control series, but also a higher incidence of rheumatoid arthritis. For example, among the 1,445 first-degree relatives of the rheumatic fever index cases the incidence of rheumatoid arthritis was 2·6% compared with 0·4% among the 1,449 first-degree relatives of the controls. Conversely the relatives of the patients with rheumatoid arthritis not only had a higher incidence of rheumatoid arthritis, but also a higher incidence of rheumatic fever than the relatives of the controls. The incidence of rheumatic fever was 4·3% among the 1,163 first-degree relatives of the patients with rheumatoid arthritis, and 2·2% for the 1,695 first-degree relatives of the controls.

The authors conclude that rheumatic fever and rheumatoid arthritis are expressions of the same genetic predisposition and suggest that a single dominant gene of variable manifestation is concerned.

[No attempt was made to match or correct for age in this survey.] *C. O. Carter*

Public Health and Industrial Medicine

220. **Poliomyelitis Studies in an Isolated Scottish Community**

A. D. MACRAE. *British Medical Journal* [*Brit. med. J.*] 1, 368–372, Feb. 16, 1957. 1 fig., 10 refs.

The author describes a search for evidence of poliomyelitis infection in an isolated community of 294 people living in 104 houses on the northern shores of Upper Loch Torridon in Ross-shire. Families with one or more children lived in 28 of the houses and the children attended schools in the area until the age of 11 years. There were few facilities for visitors to the area, which was approached by a single road from a town some 12 miles away. No cases of clinical poliomyelitis have been reported from this area, but in the summer and autumn of 1951 13 cases of Bornholm disease were notified; this disease was then prevalent in Ross-shire.

Specimens of blood or faeces or both were sought from a sample of the population in the spring (mid-March–mid-May) and again, where possible, in the autumn (mid-October–mid-December) of 1951, the method of sampling being described. Specimens were thus obtained in both spring and autumn (1) of both serum and stools from 14 children (under 16 years) and 11 adults, (2) of stools only from 7 children, and (3) of serum only from 3 children and 20 adults. In addition specimens of serum or stools were obtained in spring only from 6 children and 3 adults. In all, specimens were available from 64 persons living in 53 houses. Thirteen of the children and 6 of the adults gave further blood specimens in the autumn of 1954. The laboratory methods used in the virus investigations are described in detail. No virus was isolated from the faecal samples collected in the spring of 1951, but strains of Coxsackie virus, Group B, Type 3, were identified in samples from 5 children and strains of poliomyelitis virus, Types 2 and 3, in samples from another child in the autumn. All these children lived in different houses and were under the age of 6 years.

The presence of antibodies to the poliomyelitis viruses and their distribution in the various age groups were studied in samples of serum obtained from 55 subjects in the autumn of 1951. Although the numbers available in each age group are small, the results do suggest that immunity develops late in life. [The author distinguishes six age groups, but for present purposes the results may be regrouped to give 21 subjects under 16 years, 15 aged 16 to 50 years, and 19 aged 51 to 91 years; of these, 24, 27, and 84% respectively had Type-1 antibodies, 29, 60, and 74% had Type-2, and 5, 33, and 84% had Type-3 antibodies in their blood.]

From the limited data available in 1954 no evidence was obtained of any great variation of antibody levels in those subjects whose blood contained antibodies in 1951, but the following cases are of interest. The boy (aged 13 months in 1951) from whom poliomyelitis virus Types 2 and 3 were isolated in 1951 had antibodies to both in his serum in 1956. His sister, who was 4 years older, developed antibodies to Type 2 between the spring and autumn of 1951 and to Type 3 between 1951 and 1956. A boy (aged 10 years in 1951) who lived nearby developed antibodies to Type 2 between 1951 and 1954 and a girl aged 9 years in 1951, who had then a high antibody titre to Type 2, showed a 75% fall in titre by 1954.

In 12 serum samples taken in autumn, 1951, antibodies to Coxsackie B3 virus were present. Six came from children, and 5 of these were of school age and attended the same school. In all the children and one adult the antibodies developed between the spring and the autumn of 1951, but in 3 adults the antibodies were present in the earlier samples. In 1954 10 persons, 6 of whom gave negative reactions in 1951, were found to have such antibodies, and the author discusses their results against the background of the outbreak of Bornholm disease in Ross-shire in 1951. *E. A. Cheeseman*

221. **Canicola Fever in Man Through Contact with Infected Pigs**

J. D. COGHLAN, J. NORVAL, and H. E. SEILER. *British Medical Journal* [*Brit. med. J.*] **1**, 257–261, Feb. 2, 1957. 11 refs.

The authors describe 5 cases of leptospirosis in man due to *Leptospira canicola*, diagnosed on clinical and serological evidence, occurring between 1950 and 1955 among workers on pig farms in the neighbourhood of Edinburgh. Infection with *L. canicola* is usually supposed to be associated with dogs, but at least one previous outbreak, in South Georgia, U.S.A., was traced to swine. The present account suggests that pigs may be more frequently infected with *L. canicola* than is commonly supposed, although this is the first example of human infection traced to this source to be recorded in Great Britain.

The first case observed clinically was that of a man employed at a piggery who was admitted to hospital with a feverish illness of 8 days' duration with severe frontal headache. His blood agglutinated *L. canicola* to a significantly high titre, and that of 4 out of 5 other workers on the same farm also gave positive agglutination reactions. The 3 dogs on the farm were examined for leptospira, but their urine was negative, and only low agglutination titres for *L. canicola*—1 in 30 and 1 in 100—were obtained with blood from 2 of the dogs, while none of their sera agglutinated *L. icterohaemorrhagiae*. An examination of the pigs showed that 46 out of 75 (61%) were infected with *L. canicola*, and sera from 12 others gave a low degree of agglutination. Inquiries were extended to 10 other piggeries, and 10 out of 31 workers whose blood was examined gave positive agglutination reactions against *L. canicola*, with records of illness in most cases that may have been due to this organism.

Five pigs, 2 to 3 months old, were inoculated in various ways with a virulent culture of *L. canicola*. The 3 exposed to subcutaneous or scarification inoculation gave agglutination titres of 1 in 10,000 or higher within 10 days, while the animal exposed to infection by mouth gave negative reactions after 10 days, but gave a titre of 1 in 300 after 28 days, rising to 1 in 3,000 after 40 days. The animal inoculated intranasally showed no signs of infection. None of the pigs showed any apparent symptoms of disease, and attempts to recover the organisms, both by cultural methods and by inoculation of hamsters, were all negative. Non-infected pigs were introduced into 2 pens of an infected piggery, and in one pen all the 3 pigs introduced became infected within 6 to 8 weeks. The findings in those in the other pen were doubtful in one case and negative in 2. Urine taken from the floor of the first pen was found to contain numerous leptospires—up to 4 per field—when examined by dark-ground microscopy. The urine was injected into 2 hamsters, both of which died after 6 and 8 days respectively with no obvious symptoms and with no detectable lesions on microscopical examination, but from the heart blood an organism was cultured which was identified at the Wellcome Research Laboratories as *Leptospira canicola*. Two pigs inoculated with infected urine developed febrile symptoms and both developed high antibody titres by the 11th day. When killed on the 22nd day no abnormalities were observed, but cultures were positive and hamsters were infected by the inoculation of blood or tissues from these pigs.

The evidence indicates that pigs may harbour this infection without showing any obvious symptoms of disease, and that human infections may result from contact with infected pigs. *Edward Hindle*

222. **Epidemic Vomiting. A Study of Several Outbreaks**

G. P. McLAUGHLAN. *Medical Officer* [*Med. Offr*] **97**, 47–53, Jan. 25, 1957. 5 refs.

The author presents a study of 6 outbreaks of epidemic vomiting which occurred in 1955 in Exeter, of which 3 were "school outbreaks"—in a nursery school, a junior school, and a residential school for the deaf respectively—each showing a different pattern, and the others were "family outbreaks".

Among 37 children attending the nursery school, only 9 were affected and, in contrast to the usual pattern, the infection spread slowly and the outbreak extended over 9 days. The outbreak in the junior school affected 78 children aged 7 to 11, 2 teachers, and 3 of the kitchen staff. Here the onset was explosive in character, 31 of the cases occurring on the first day and new cases developing during the 2 succeeding days; 12 secondary cases occurred in the homes of affected children during the outbreak, and the findings in these cases suggested that the incubation period ranged from 24 to 72 hours. In the (mainly) residential school, although 130 of the children were living together, only 14 children were affected, all of whom were residential; no day pupils (13) or members of staff (36) were affected. The temperature of the patients in this last outbreak ranged from 99° to 100° F. (37·2° to 37·8° C.), with one exception (101·4° F.; 38·5° C.). In no instance was the vomiting followed by diarrhoea, nor were there any other symptoms, in contrast to the other two outbreaks in which the symptoms included diarrhoea, abdominal discomfort, and severe headache. The three family outbreaks affected respectively: 2 adults and one child in one family, 3 adults and 3 children in two families, and 4 adults in two families; the chief symptoms here were nausea, vomiting, and diarrhoea.

The present series did not include any instance of giddiness or of upper respiratory symptoms, which have been recorded in previous outbreaks. A study of the infectivity suggested that the virus in the nursery-school outbreak was much less virulent than that in the other two school outbreaks. The diagnosis of epidemic vomiting is usually based on the symptoms, the pattern of the outbreak, and the negative bacteriological findings. The possibility of staphylococcal enterotoxin must be borne in mind in investigating such outbreaks, although often any relationship of the symptoms to the taking of food is lacking. *R. G. Meyer*

223. **Some Demographic and Vital Statistics of the USSR.** (Некоторые демографические и санитарно-статистические данные о СССР)

A. M. MERKOV. *Гигиена и Санитария* [*Gigiena*] 6–12, No. 1, Jan., 1957.

[This article gives a large amount of factual information which is extremely interesting but which cannot easily be summarized. A few extracts from the data provided are given below.]

The area of the U.S.S.R. is 22,403,000 sq. km., or 16·6% of the land surface of the globe. The population of the U.S.S.R. was 200·2 millions in April, 1956; this is 7·5% of the population of the world. The population of the 10 largest towns is given, headed by Moscow with a population of 4,839,000, excluding suburbs. The numbers of births and deaths and the natural increase of the population for various years since 1913 are noted and are compared with such data for other countries. Urban living accommodation totalled 640 million sq. metres in 1955, giving 7·4 sq. metres per head. The rate of building during various periods since 1918 is given.

Out of a total working population of 48,338,000, the health services employed 2,627,000 (5·4%); 45% of all workers, and 85% of health-service workers, are women. These figures are exceeded only by teachers and cultural workers and by engineers. The number of doctors (including dentists) in 1955 was 333,800, and is now 1 per 605 persons or 16·7 per 10,000. The distribution in the various republics is given and compared with that in other countries. It is claimed that the proportion of doctors to population in the U.S.S.R. is the highest in the world (England and Wales, 9·1 per 10,000). There were 223,900 qualified scientific workers in October, 1955. The total number of students was 33,998,000 (17% of the population).

In 1955 the total number of hospital beds in the U.S.S.R. was 1,290,200 or 6·45 per 1,000 population. (England and Wales 10·8 per 1,000.) The low figure

compared with capitalist countries is explained by the fact that in such countries many beds are restricted to those sections of the community who can pay, and that many of them are in mental hospitals, for which there is not the same need in the U.S.S.R. Day nurseries provided 906,000 places and kindergartens 1,713,000 places in 1955. In addition there were 2,000,000 places for children in holiday nurseries. *Basil Haigh*

INDUSTRIAL MEDICINE

224. **The Treatment of Tetraethyl Lead Poisoning**
P. R. Boyd, G. Walker, and I. N. Henderson. *Lancet* [*Lancet*] **1**, 181–185, Jan. 26, 1957. 2 figs., 22 refs.

Four non-fatal cases of tetraethyl lead poisoning seen at the Middlesex Hospital, London, are described, the patients being men who had worked for 6 weeks cleaning tanks which had contained leaded petrol. Full details are given of 3 cases, the severity of the toxic psychosis in the fourth case preventing careful biochemical observation. As in previously reported cases the main clinical features were psychiatric, their form depending on the underlying personality of the patient. In all cases there was mild hypotension and, before treatment, the urinary and faecal excretion of lead was increased. Intravenous infusion of sodium calciumedetate (" edathamil $CaNa_2$ ") (1 g. per 30 lb. [13·6 kg.] body weight) resulted in a sevenfold increase in urinary excretion of lead, but oral administration of this drug and of penicillamine was ineffective. The results obtained with sodium calciumedetate were not as dramatic in these cases as in cases of poisoning with inorganic lead.

The fourth patient became violent, making drug treatment at first impossible. There was an improvement, however, with electric convulsion therapy (E.C.T.), and sodium calciumedetate was given. The authors refer briefly to the use of E.C.T. as an adjuvant in the treatment of toxic psychoses. *H. B. Stoner*

225. **Hygienic Working Conditions in Polyvinyl Chloride Tar Plants.** (Санитарно-гигиенические условия труда в производстве полихлорвиниловой смолы и меры их оздоровления)
V. S. Filatova and E. S. Gronsberg. *Гигиена и Санитария* [*Gigiena*] 38–42, No. 1, Jan., 1957. 4 refs.

The occurrence of angioneuroses of a spastic type has been described elsewhere among workers at polyvinyl chloride (PVC) tar plants, for which inhalation of vinyl chloride was held responsible. In this article the authors describe investigations of the concentration of vinyl chloride in the atmosphere in various parts of such a plant. The method of estimation used, that of Gronsberg, depends on the treatment of solutions of vinyl chloride in chloroform with a solution of bromine in a mixture of chloroform and glacial acetic acid in the presence of light. The manufacturing process entails the polymerization of vinyl chloride by means of a catalyst (benzoyl peroxide) and an emulsifying agent (industrial gelatin), applied at a temperature of 48° to 52° C. and a pressure of 7·5 to 9 atmospheres for 24 to 36 hours. This produces a PVC tar which is treated with alkali at a temperature of 90° to 96° C., centrifuged, and dried in ovens at 90° C. The finished product is packed in paper bags.

The investigation showed that vinyl chloride was present in varying concentrations in the air in all parts of the plant, but especially where dust from the dry product was a complicating factor. The average concentration found was 0·05 to 0·8 mg. per litre which is below the maximum allowable concentration (1 mg. per litre) of the State Sanitary Inspectorate. Installation of exhaust ventilation, replacement of manually discharged by semi-automatic centrifuges, and the building of a new drying system reduced the vinyl chloride concentration in the environment to between 0·01 and 0·04 mg. per litre. In spite of this the occurrence of angioneuroses has continued, suggesting that the present value for the maximum allowable concentration of vinyl chloride is too high. *Basil Haigh*

226. **Clinical Study of Pneumoconiosis of Coal Workers in Ohio River Valley**
M. D. Levine and M. B. Hunter. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **163**, 1–4, Jan. 5, 1957. 14 refs.

The pattern of respiratory illness in 60 miners in whom there was radiological evidence of coalworkers' pneumoconiosis was studied over a 2-year period, and the findings are discussed in this paper from Bellaire Clinic, Ohio. Altogether 153 miners were seen during this period with radiological signs of pneumoconiosis, and the 60 studied were free from non-respiratory cardiac disease. A group of 74 miners matched for age but free from pneumoconiosis served as controls.

Dyspnoea, cough, and emphysema (diagnosed chiefly on radiological criteria) were more frequent in miners with pneumoconiosis than in those without. Treatment was on standard lines. The authors emphasize the importance of the radiological technique in the diagnosis of pneumoconiosis. In their view properly designed surveys are necessary to determine the true incidence and the significance of the disease in the United States. It is of interest that one patient in the series with massive fibrosis was tuberculin-negative. *C. M. Fletcher*

227. **Foot Ringworm in Coal-miners**
J. C. Gentles and J. G. Holmes. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **14**, 22–29, Jan., 1957. 1 fig., 27 refs.

An epidemiological survey of ringworm of the foot was carried out among 2,101 subjects in widely separated areas in Great Britain, including 11 pits, a training centre, and two power stations. Of these, 1,900 had some clinical abnormality of the skin of the feet Ringworm infection, however, was found in only 438 (20·8%), and in 5 of these the feet were clinically normal. The diagnosis was confirmed by culture and histological examination in 346, by culture only in 57, by microscopy only in 32, and by other methods in 3. The organisms found on culture were *Trichophyton mentagrophytes* in 244, *T. rubrum* in 148, and *Epidermophyton floccosum* in 11.

While the over-all species distribution was *T. mentagrophytes* 61%, *T. rubrum* 35%, and *E. floccosum* 4%, in the multiple infections the percentages were 80, 85, and 35 respectively. The incidence, as judged by the laboratory findings, varied from 3·5% to 50%. Variation, however, was not related to geography, since in two neighbouring areas the incidence was respectively 12% and 50%. Communal baths appeared to be the most important factor. The incidence among men who used communal baths was 31% (364 out of 1,153) and among others it was 8% (74 out of 948). There were no baths at 4 pits, and the incidence in these ranged from 6% to 15%; at pits and power stations with baths the incidence ranged from 16% to 50%. None of the men was off work primarily because of a skin complaint, but 2% gave a history of "lost time" for conditions diagnosed as foot ringworm by their own doctors. There did not appear to be any seasonal variation in the incidence of ringworm of the foot. Discussing the view of some other workers that ringworm infection of the foot depends on personal immunity, while exposure is unimportant, the authors state that "it is difficult to see why only communal bathing should lead to a breakdown in immunity". The findings in men who used communal baths, among whom the incidence was high, showed that the species distribution was peculiar to the particular pit. Dermatophytes were cultured from the floors of 4 bath-houses, and on each occasion the species cultured corresponded to that found on the majority of the men.

It is concluded that fungus infections of the feet are not universal; that a specific exposure and a breakdown in personal immunity are necessary for infection to occur; and that in Great Britain these conditions are most commonly found together in those who use communal baths. *Kenneth M. A. Perry*

228. **The Prevalence of Tuberculosis at Necropsy in Progressive Massive Fibrosis of Coalworkers**
D. Rivers, W. R. L. James, D. G. Davies, and S. Thomson. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **14**, 39–42, Jan., 1957. 19 refs.

The results of necropsy examination, both by culture and by animal inoculation, for the presence of tubercle bacilli in 153 cases of pneumoconiosis occurring in South Wales coal-miners are reported. These cases formed part of the routine post-mortem material seen during the years 1952–4, and included 118 cases of progressive massive fibrosis, which were the special object of the study. Swabs from the bronchus were immersed in 2·5% oxalic acid for 45 minutes, and then rubbed over the surface of Löwenstein–Jensen medium (two tubes). The fibrous mass and hilar gland were blended with 20 ml. of nutrient broth in a Waring blender for 2 minutes at 15,000 r.p.m. The tissue thus macerated was treated with an equal volume of 4% caustic soda for 30 minutes at 37° C This produced homogenization of the mush, which was then diluted with 25 ml. of sterile water and centrifuged at 3,000 r.p.m. for 30 minutes. The deposit was neutralized with 3% hydrochloric acid, and cultures were then made from this on Löwenstein–Jensen or Kirschner's medium; a guinea-pig was also inoculated. By these two methods tubercle bacilli were isolated from 41 cases (35%).

In all cases two or more blocks of tissue from the lesions in each lung were taken for histological examination, sections being stained with haematoxylin and eosin. Tuberculosis was diagnosed only if all the classic features were present. Naked-eye or histological evidence of tuberculosis was recognized pathologically in 31 of the above 41 cases—that is, in 28% of the total.

The authors conclude that there is a marked difference between the prevalence of tuberculous infection as shown by a necropsy study and that found during life among cases of progressive massive fibrosis. Thus Cochrane *et al.* (*Brit. med. J.*, 1952, **2**, 843; *Abstracts of World Medicine*, 1953, **13**, 282) obtained only 1·1% of positive results by laryngeal swabbing, and Kilpatrick *et al.* (*Thorax*, 1954, **9**, 260; *Abstracts of World Medicine*, 1955, **17**, 510) found tubercle bacilli in sputum examined by culture and guinea-pig inoculation in only 7·7% of cases. It appears, therefore, that open tuberculosis is present at death in about one-quarter of cases of progressive massive fibrosis; whether or not the tuberculous infection occurs early or late could not be deduced from this study. *Kenneth M. A. Perry*

229. **Decompression Sickness during the Sinking of a Caisson. A Study of Some Factors in the Pathogenesis of Caisson Disease**
H. E. Lewis and W. D. M. Paton. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **14**, 5–12, Jan., 1957. 4 figs., 3 refs.

In 1950, during the sinking of reinforced concrete caissons in the Thames, 89 cases of decompression sickness ("bends") were encountered among 1,800 compressions at the inlet caisson and 310 decompressions at the outlet caisson. The legs were frequently affected and usually the manifestations were bilateral. Two men suffered from as many as 6 attacks each. Contributory factors included faulty decompression, cooling of the atmosphere, condensation of moisture on the men's clothes, and vitiation of the air by carbon dioxide. Exercise was also believed to be of aetiological importance, for the men had to climb a long ladder in order to reach the decompression lock. The maximum pressure employed was about 35 lb. per sq. in. (2·4 kg. per sq. cm.), but the pressure varied with the tide by at least 10 lb. per sq. in. (0·7 kg. per sq. cm.).

To safeguard against inaccurate decompression the authors recommend that lock-keepers should be properly trained and that a recording barograph should be installed where decompression takes place. The blister lock should be ventilated adequately, for overcrowding of the lock leads to the accumulation of significant amounts of carbon dioxide. After climbing the caisson ladder the men should wait for 10 minutes in order to reduce the effect of exercise and to allow their carbon dioxide production to sink to resting levels. Rapid ascents probably create nuclei for the formation of bends in the muscles. Dry clothes should be provided and the lock should be kept warm throughout the course of decompression. *A. Garland*

Anaesthetics

230. **The Complications of Hydroxydione Anaesthesia**
A. R. HUNTER. *Anaesthesia* [*Anaesthesia*] **12**, 10–14, Jan., 1957. 1 fig., 8 refs.

The author of this paper from the Royal Infirmary, Manchester, is concerned to show from his own experience that the action of hydroxydione (" viadril "; 21-hydroxypregnanedione sodium hemisuccinate) cannot be equated with that of other anaesthetic drugs, such as the barbiturates or pethidine, which are also given intravenously for the same purpose. Hydroxydione was administered to 24 patients by slow intravenous drip. In 11 who received only 500 mg. a supplementary dose of a barbiturate was necessary to complete the induction before continuing with nitrous oxide. There were no side-effects attributable to the steroid. Of the remaining 13 patients who received doses of hydroxydione ranging from 670 to 1,000 mg., only 2 required a barbiturate as well for induction, but in 12 of them there was a steady fall in blood pressure, which continued for as long as 45 minutes after completion of induction. In 2 of the latter group disturbances of respiration attributable to hydroxydione occurred about 10 minutes after completion of induction. These took the form of inefficient paradoxical movements which were not corrected by assisted respiration, administration of either methylamphetamine or nikethamide being necessary for restoration to normal rhythm and pattern.

It is thus apparent that with hydroxydione there is a very slow, 25-minute induction, but it is not possible to " titrate " the drug against the patient's requirements and a very nice judgment of the appropriate dosage is necessary. *Donald V. Bateman*

231. **Observations on Trifluoroethylvinyl Ether**
J. W. DUNDEE, H. W. LINDE, and R. D. DRIPPS. *Anesthesiology* [*Anesthesiology*] **18**, 66–72, Jan.–Feb., 1957. 2 figs., 5 refs.

The authors have investigated, at the University of Pennsylvania, the anaesthetic properties of trifluoroethylvinyl ether (" fluoromar ") in 300 administrations for general surgical, gynaecological, urological, orthopaedic, otolaryngological, and dental operations on patients of all ages and both sexes.

Open drop induction was found to be slow and unsatisfactory, probably owing to the high boiling point (42·7° C.) of the drug, but it could easily be introduced into a semi-closed or closed system following nitrous oxide and oxygen. Changes in the depth of anaesthesia occurred rapidly, so much so that the signs and stages of anaesthesia as described by Guedel were inapplicable, respiratory paralysis sometimes occurring before eyeball movements ceased. Electroencephalographic changes were similar initially to those described for diethyl ether, but once anaesthesia was established its depth was harder to assess. In 12 cases surgical anaesthesia occurred at Levels 2 to 3, deep anaesthesia at Levels 4 to 5, and apnoea between Levels 5 and 7. Determination of the blood level of the anaesthetic in 22 patients showed progressive depression from 15 mg. per 100 ml. in Plane-I anaesthesia to 50 mg. per 100 ml. when apnoea was present. Spirometric tracings (reproduced with this paper) show the ease with which respiratory depression occurs and can be reversed. In patients not premedicated with opiates, tachypnoea was frequent, but could be reduced by the intravenous infusion of 10 to 20 mg. of pethidine hydrochloride.

In 25% of the cases a fall in blood pressure was associated with deep anaesthesia, the degree of fall showing correlation with increasing blood levels of the anaesthetic. Electrocardiographic studies on 11 patients at levels of anaesthesia, as determined electroencephalographically, varying from 2 to 7 showed transient nodal displacement in light anaesthesia in 3 cases, tachycardia in 3, and temporary inversion of the T wave in Lead II in one patient in deep anaesthesia. Muscular relaxation was generally good and recovery very rapid, only 5 out of 280 patients taking longer than 30 minutes to recover completely their mental faculties. The manufacturers state that the lower limit of inflammability of this drug is 4% in oxygen. Other workers have reported analgesia with inspired concentrations of 1·2 to 2·0 volumes per cent. It is compatible with any of the carbon dioxide absorbents.

The authors point out that among the useful properties of this drug are its low inflammability, its compatibility with soda lime, and the rapid induction and recovery it provides. The disadvantages include its liability to produce respiratory depression with acidosis, and tachypnoea in patients who have not received premedication [drawbacks which would seem to outweigh the advantages of this drug]. *Raymond Vale*

232. **Effect of Cyclopropane Anesthesia on Cardiac Output and Related Hemodynamics in Man**
TUSUNG-HAN LI and B. ETSTEN. *Anesthesiology* [*Anesthesiology*] **18**, 15–32, Jan.–Feb., 1957. 4 figs., bibliography.

In view of previous conflicting reports on the action of cyclopropane in man, its influence on cardiac output and related haemodynamics was investigated in the study here reported from Indiana University School of Medicine, Indianapolis, in which 35 determinations in all were made on 14 patients aged 16 to 61 undergoing surgical operations. After a standard premedication one to 2 hours previously, 100% oxygen was given to eliminate nitrogen from the lungs before inducing anaesthesia with cyclopropane and oxygen in a closed circuit with to-and-fro absorption. Breathing was spontaneous throughout. Different levels of anaesthesia were induced, as assessed by the electroencephalographic find-

ings and the blood cyclopropane concentration, each level being maintained for 30 minutes before determination of the cardiac output (by a dye dilution method), the arterial blood pressure (using a Statham strain gauge), heart rate, mean circulation time, arterial blood oxygen and carbon dioxide content (by Van Slyke's method), and the *p*H of the blood. From this information the total peripheral resistance, stroke volume, left ventricular output, and the intrathoracic blood volume were calculated. The haematocrit was determined by centrifuging in Wintrobe tubes and the blood cyclopropane concentration by the method of Orcutt and Waters.

The right auricular pressure, which was measured in 4 cases under light anaesthesia, showed a rise from a mean of 2·5 to a mean of 10·2 cm. H_2O. The mean cardiac index during the resting state was 3·32 litre per minute per sq. metre, which compares well with previous observations by other workers. In light anaesthesia this index fell to 2·49, in deep anaesthesia to 2·96, and in very deep anaesthesia to 3·12 litre per minute per sq. metre, the fall in cardiac output being correlated with the fall in pulse rate. The index of intrathoracic blood volume under anaesthesia showed no significant change from the resting level. Of 25 determinations, the stroke volume showed an increase in 10, a decrease in 5, and no significant change in the other 10. The mean arterial blood pressure showed an increase under anaesthesia, while the total peripheral resistance rose during light anaesthesia by 46%, during deep anaesthesia by 30%, and during very deep anaesthesia by 16%. There was no significant change in the ventricular work. The mean circulation time rose under anaesthesia, and the pCO_2 rose in the deeper planes of anaesthesia with a corresponding fall in the blood *p*H, both these changes being due to respiratory depression; the rise in pCO_2 was not correlated with the fall in cardiac output.

The authors discuss the factors responsible for these changes and point out that the changes are strikingly similar to those produced by intravenous infusion of noradrenaline. They conclude that the function of the heart is not impaired by surgical anaesthesia with cyclopropane. *Raymond Vale*

233. Comparison of an Ultrashort Acting Barbiturate (22451) with Thiobarbiturates during Anesthesia

C. M. GRUBER, V. K. STOELTING, R. B. FORNEY, P. WHITE, and M. DEMEYER. *Anesthesiology* [*Anesthesiology*] **18**, 50–65, Jan.–Feb., 1957. 3 figs., 9 refs.

In a study carried out at the Indiana University Medical Center, Indianapolis, as part of a search for an ultrashort-acting oxygen barbiturate, the action of a stereoisomeric mixture of alpha and beta DL-1-methyl-5-allyl-5-(1-methyl-2-pentynyl) barbituric acid sodium salt (Compound 22451) was investigated and compared with that of thiopentone and of " thioseconal ". This compound is soluble in water, forming a stable solution of *p*H 10 to 11. After the rapid intravenous infusion of 100 mg. of Compound 22451 and of 500 mg. of thiopentone into 5 healthy volunteer subjects on separate occasions, the plasma barbiturate level was determined by ultraviolet spectrophotometry, the timing being recorded on a continuous electroencephalographic (EEG) tracing. The reappearance of pre-anaesthetic EEG wave forms and clinical signs of recovery occurred earlier with Compound 22451 than with thiopentone, as did also a return to a normal EEG pattern and clinical picture.

The consistent EEG pattern observed after administration of barbiturates suggested a similar study with Compound 22451. To each of 5 volunteers intravenous infusions of 100 mg. of Compound 22451 and of 500 mg. of thiopentone were given as rapidly as possible (at 48 hours' interval). In another 5 volunteers Compound 22451 was given slowly at the rate of 30 mg. per minute and thiopentone at 100 mg. per minute to average doses of 100 mg. and 500 mg. respectively. In both groups the electroencephalogram was recorded continuously from before administration until complete recovery, and estimates of the clinical level of anaesthesia were correlated with these. In the group given the drugs rapidly Compound 22451 produced EEG wave forms similar to those seen in some types of convulsive disorder, although no actual convulsion occurred. The initial changes were noted 13 seconds after infusion (the changes are illustrated in EEGs reproduced). The typical fast activity associated with administration of barbiturates was not observed, and except for this and the predominant waves of 12 to 15 c.p.s., the EEG records for the two drugs were similar. After slow infusion of the drugs the sudden initial changes were absent, but otherwise the EEG records showed little difference. The onset of and recovery from anaesthesia were faster in all cases with Compound 22451 than with thiopentone.

Compound 22451 was then compared with thioseconal and thiopentone as to their effect in modifying electric convulsion therapy in 50 psychotic women patients, the double-blind technique being employed. The dose needed to produce anaesthesia in 50% of the patients was 22·3 mg. of Compound 22451, 138 mg. of thiopentone, and 125 mg. of thioseconal. Thus Compound 22451 is about six times as potent as these thiobarbiturates. Finally Compound 22451 was given intravenously to 650 patients as an anaesthetic for surgery, and the results compared with those from the records of a similar number of patients who had received thiopentone or thioseconal. The average dose of Compound 22451 was 54·4 mg., the equivalent doses for thiopentone and thioseconal being 2·5 and 4 times as large respectively. Determination of the regression equation for the duration and dose of Compound 22451 when given intermittently with a 3:1 mixture of nitrous oxide and oxygen to 187 patients showed that it is used at a rate of 57 mg. per hour. Similar equations for thiopentone and thioseconal gave rates of 58 and 153 mg. per hour respectively. When a 0·1% solution of the compound was given by continuous drip much larger quantities were used, the regression equation indicating a rate of use of 95 mg. per hour. The main complications, namely, muscular twitching and hiccup, occurred more frequently than with the other drugs and investigations of the alpha isomer, with which these are said not to occur, are continuing. All the patients awoke very promptly when the compound was discontinued and were surprisingly alert. *Raymond Vale*

Radiology

234. **Cardiac Ventriculography. Direct Transthoracic Needle Puncture Opacification of the Left (or Right) Ventricle.**
J. S. LEHMAN, B. G. MUSSER, and H. D. LYKENS. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] 77, 207–234, Feb., 1957. 18 figs., 9 refs.

From Hahnemann Medical College and Hospital, Philadelphia, the authors describe a method of cardiac ventriculography in which the contrast medium is introduced into the ventricles by direct transthoracic needle puncture; their observations are based on the experience gained in 77 examinations carried out on 61 patients. Premedication to allay apprehension is advocated. Rapid serial exposure of the films at the rate of 2 per second for 6 seconds is necessary during and after the injection of the medium, pressure tracings recorded by a capacitance-type electromanometer and electrocardiographic changes being continuously observed. For the puncture a 6-inch (15-cm.) short-bevelled needle, Gauge 18, is used, this being attached to a length of polyethylene tubing with a lumen 2 mm. in diameter in which is incorporated a Luer-Lok three-way stopcock to one branch of which the electromanometer is connected. Through a 50-ml. syringe furnished with a mechanical pressure injector 50 ml. of opaque material (70% diodone) is injected in 2 seconds or less.

All examinations were carried out in the horizontal position. An exaggerated right posterior oblique projection was found to be the best for identifying mitral valve insufficiency, sometimes with a caudal tube angulation of 15 degrees. This position was also the best for demonstrating aneurysms arising from the posterior wall of the left ventricle and lesions of the aorta and aortic valve. An antero-posterior projection is recommended for visualizing signs of tricuspid insufficiency and aneurysms arising from the antero-lateral wall of the left ventricle. A preliminary film is taken after a strip of lead numerals 1 cm. apart have been affixed to the patient's skin in the area of radiological projection of the ventricle as an aid in directing the needle. Puncture is made in the xiphoid area after local analgesia has been induced with procaine. For left ventriculography the needle is inserted towards the left at an angle of 10 degrees to the sagittal plane. If the left ventricle is enlarged or displaced by a large right ventricle the angle should be approximately 20 degrees. For the right ventricle the needle is aimed at the estimated centre of the right ventricle, but directed nearer to the sagittal axis. If after puncture the recorded pressure is lower than the systemic blood pressure it may be assumed that the needle is within the right ventricle. The patient is instructed to stop breathing at the time of injection, and he must also be cautioned against taking a deep breath during and following insertion of the needle. The needle should be inserted rapidly and withdrawn immediately after the injection. In 3 out of 69 examinations for left ventriculography the right ventricle was entered unintentionally; which ventricle has been entered can usually be confirmed by allowing blood to flow back into the tubing and noting the degree of oxygenation. It is essential to be certain that the needle tip is well within the ventricular cavity. Of the 77 examinations, 13 were classified as failures; the cause of failure was injection of the wrong ventricle in 4 cases, needle tip too high in the outflow tract in 3, accidental intramyocardial or intrapericardial injection in 3, and breakage of the syringe, failure of the serial apparatus, and wrong positioning of the patient each in one case. Of the remaining examinations the results were adjudged to be "excellent" in 32, "good" in 21, "fair" in 7, and "poor" in 4. The reactions were similar to those experienced with angiocardiography, except that with left ventriculography they were somewhat more pronounced. Of the cases in which there was intramyocardial injection of diodone complete heart block developed in one.

John H. L. Conway-Hughes

235. **Roentgenologic Aspects of the Eisenmenger Complex**
C. L. EBNOTHER and H. L. ABRAMS. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] 77, 248–262, Feb., 1957. 10 figs., 35 refs.

The authors present the radiological findings in 12 cases of the Eisenmenger complex studied at Stanford University School of Medicine, San Francisco. In all cases cardiac catheterization, measurement of intracardiac and pulmonary arterial pressures, and oxygen saturation studies were carried out. The age of the patients ranged from 4 to 34 years and the sex distribution was equal; in all of them cardiac or respiratory disease had been suspected at birth or soon after because of cyanosis. A history of recurrent pulmonary infection was obtained in two-thirds of the cases.

Radiologically, the over-all size of the heart in the postero-anterior projection was not increased; right ventricular enlargement was present to some degree in all cases, but left ventricular enlargement was not a striking feature. In 8 of the cases there was suggestive evidence of right atrial enlargement, whereas the size of the left atrium was normal in all but one case. In 2 of the patients followed over a period of 4 years there was a definite decrease in over-all heart size with increasing age. The main pulmonary artery, as judged by the relative prominence of the pulmonary artery segment of the left border of the heart shadow, was enlarged in all instances, and grossly dilated in 8 of the 12 cases. The central pulmonary arteries, measured as the widest point of the right descending pulmonary artery, were consistently enlarged, markedly so in 8 of the cases. Vigorous pulsation of the main and central pulmonary arteries was observed in most instances. The mid-zone

pulmonary branches were more prominent than normal in most cases. The peripheral branches in all but one case were disproportionately small in relation to the calibre of the enlarged hilar vessels. The aorta appeared to be hypoplastic in 9 cases, but this was probably due to the fact that the enlarged main pulmonary artery obscured the aortic knob.

The authors believe that a study of the radiological appearances combined with the clinical findings will frequently enable a specific diagnosis to be made, but a number of other lesions must be considered in the differential diagnosis. They point out that even after cardiac catheterization, if the catheter has failed to enter the pulmonary artery, the diagnosis may not be established. Angiocardiography may be of help, but failure to demonstrate an overriding aorta does not necessarily exclude this anomaly. In patients with large left-to-right shunts and normal pulmonary pressure the main and hilar arteries are enlarged and the peripheral arteries show a commensurate increase, as compared with patients with pulmonary hypertension in whom these arteries are narrowed. In the authors' experience post-stenotic dilatation never affects the right descending pulmonary artery. Kerley's lines were observed only in one case of the Eisenmenger complex with pulmonary hypertension. *John H. L. Conway-Hughes*

236. **The Radiological Diagnosis of Pulmonary Embolism**

S. ROBERTS. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **50**, 93–96, Feb., 1957. 5 figs., 3 refs.

237. **The Roentgenologic Diagnosis of Pulmonary Hypertension in Mitral Stenosis**

J. B. SCHWEDEL, D. W. ESCHER, R. S. AARON, and D. YOUNG. *American Heart Journal* [*Amer. Heart J.*] **53**, 163–170, Feb., 1957. 7 figs., 5 refs.

In order to establish an additional useful criterion for the assessment of pulmonary hypertension in cases of mitral stenosis the authors have investigated, at the Montefiore Hospital, New York, the correlation, if any, between the width of the right descending branch of the pulmonary artery as measured on the radiograph and the pulmonary arterial pressure as determined at cardiac catheterization or by direct measurement at operation. In 6-foot (1·8-m.) postero-anterior projections of the chest the translucency of the right lower-lobe bronchus is usually clearly defined. The authors measure from the outer border of this structure perpendicularly to the outer border of the shadow of the descending pulmonary artery. Examination of 100 control normal subjects aged between 40 and 60 years showed that in 90 cases this measurement on the film fell within the range of 9 to 14 mm., and in a further 100 hospital employees aged between 18 and 60 years the range in 90% was between 9 and 13 mm. The authors therefore consider a measurement in excess of 14 mm. to be abnormal.

They then examined 105 patients with mitral stenosis. Close correlation was found between measurements of 14 mm. or more and a rise in pulmonary tension to 25 mm. Hg or higher. In cases in which the measurement was 14 mm. or less there was less correlation. Also in 17 cases measurements obtained by catheter showed a significant rise in pulmonary tension, but the arterial calibre was below 14 mm. The authors therefore conclude that a normal radiograph does not exclude pulmonary hypertension, but that an abnormal measurement, that is, over 14 mm., is very suggestive of its presence. *A. M. Rackow*

238. **Radiographic Estimation of Pulmonary Artery Pressure in Mitral Valvular Disease**

G. JACOBSON, L. H. SCHWARTZ, and M. L. SUSSMAN. *Radiology* [*Radiology*] **68**, 15–24, Jan., 1957. 9 figs., 19 refs.

In this paper from Los Angeles County Hospital and the University of Southern California a radiological study is reported of 124 cases of mitral valvular disease, the object being to determine whether a clinically useful correlation could be established between the size of the pulmonary artery and its main branches and the pulmonary arterial pressure. It was found that 92% of patients with a moderate or marked enlargement of the pulmonary artery and its major branches had pulmonary hypertension. Of patients with either a normal pulmonary artery or slight enlargement, only 42% had significant hypertension. From these findings the authors conclude that if the sole reason for cardiac catheterization is to determine pulmonary arterial pressure, then this procedure is unnecessary when enlargement of the pulmonary artery segment is moderate or marked. *L. G. Blair*

239. **An Evaluation of the Roentgen Manifestations of Isolated Ventricular Septal Defect**

T. E. KEATS, V. A. KREIS, and E. SIMPSON. *Radiology* [*Radiology*] **68**, 9–14, Jan., 1957. 3 figs., 22 refs.

The electrocardiographic and radiological findings in 20 patients with isolated ventricular septal defects at the University of California School of Medicine, San Francisco, are discussed. The most characteristic *x*-ray appearance is a slightly to moderately enlarged heart with right ventricular enlargement and associated enlargement of the left ventricle and/or the left auricle. The pulmonary artery is enlarged, and there is increased pulmonary vascularity. The aorta is not increased in size. In atrial septal defect, enlargement of the left side is extremely uncommon, and this, the authors state, should help to differentiate such cases from cases of ventricular septal defect in which this enlargement is seen. In cases of patent ductus arteriosus associated with pulmonary hypertension, the radiological differential diagnosis of ventricular septal defect may be extremely difficult. In some of these there is an increase in the size of the aorta, which should help in the differentiation of ventricular septal defect. *L. G. Blair*

240. **Roentgenographic Visualization of the Coronary Arteries**

N. E. REICH and M. WITTEN. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **77**, 274–280, Feb., 1957. 7 figs., 2 refs.

241. **Portal Circulation in Portal Hypertension.** [In English]
I. BERGSTRAND and C. A. EKMAN. *Acta radiologica* [*Acta radiol. (Stockh.)*] **47**, 1–22, Jan., 1957. 5 figs., 40 refs.

At the University Hospital, Lund, Sweden, the authors have studied the portal circulation in 88 patients, of whom 54 had portal hypertension, by means of the injection of a contrast solution (sodium acetrizoate) into the body of the spleen, followed by rapid serial radiography. A collateral circulation was considered to be present when branches of the splenic or portal veins filled with contrast medium. The rate of portal blood flow was assessed by measuring the time required for the opaque column to reach certain predetermined landmarks and finally to clear the hepatic vein. A note was made of the calibre of the splenic and portal veins as measured on the radiograph.

Of the total of 115 examinations performed, 31 (including 16 on control subjects) showed no filling of collateral veins, while in 59 cases collateral filling was seen, evidence of obstruction of the flow to the liver being obtained in 21 of these cases; in the others the dye reached the liver and passed through with varying velocity, depending on the morbid process present. The collateral veins seen, in order of frequency, were the coronary vein, the short gastric veins, and the inferior mesenteric vein; the superior mesenteric was not seen. The correlation of demonstrable collaterals with the presence of portal hypertension was complete in the series investigated, occurring in all cases of portal hypertension and in none of the control cases. Oesophageal varices were demonstrated radiologically in 43 out of the 48 cases in which there was filling of collaterals as a result of chronic obstruction. The velocity of blood flow in the splenic and portal veins was found generally to be lower in the presence of portal hypertension than in the controls, and there was a tendency in these cases also for the width of the splenic and portal veins to be increased. The authors regard the method as a satisfactory and reliable one for the diagnosis of portal hypertension. *A. M. Rackow*

242. **Vertebral Changes in Childhood Leukemia**
B. S. EPSTEIN. *Radiology* [*Radiology*] **68**, 65–69, Jan., 1957. 6 figs., 8 refs.

The radiological changes in the spine of children aged 6 months to 14 years with leukaemia are described in this paper from the Long Island Jewish Hospital, New Hyde Park, N.Y. These changes included diffuse demineralization of the vertebrae, not confined to the bodies, but involving also the neural arches and transverse processes. In 6 of the 15 children examined this demineralization was greater in the centres of the vertebrae than at the periphery. Varying degrees of compression of the vertebral bodies were seen, the most common structural change being anterior wedging. In some infants the anterior venous sinuses were widened, and thinning and breaking of the cortical margins were occasionally seen. Horizontal zones of increased radiotranslucency at the upper and lower faces of the vertebral bodies, corresponding to similar zones at the ends of the long bones, were observed in a number of instances.

The extent of vertebral demineralization in 7 cases coming to necropsy varied considerably, but appeared to be more pronounced in the middle and lower thoracic and upper lumbar regions. *L. G. Blair*

243. **Radiographic Appearances in the Wrist in Early Rheumatoid Arthritis.** (Images carpiennes du début de la polyarthrite)
L. ISEMEIN and A. M. FOURNIER. *Journal de radiologie, d'électrologie et Archives d'électricité médicale* [*J. Radiol. Electrol.*] **37**, 869–876, Nov.–Dec., 1956 [received Feb., 1957]. 10 figs.

The authors describe the earliest changes observed in rheumatoid arthritis in the carpal bones and illustrate them in a series of radiographs. These changes may occur before involvement of the articular surfaces and sometimes even before the onset of any clinical symptoms. They consist in cystic areas within the bones, sometimes with opaque areas, and in other cases a diffuse osteosclerosis is seen. The carpus may show a gradual slipping towards the ulnar margin, while eventually the semilunar may be almost in contact with the styloid process of the ulna. The appearance of the carpal bones in a young adult may come to resemble that of an old man. In one of the authors' cases these early changes were present for 5 years before the onset of symptoms, but when symptoms eventually appeared there was rapid progression of the disease, with advanced radiological changes. *John H. L. Conway-Hughes*

244. **Structural Disorders and Destructive Lesions of Bone in Ankylosing Spondylitis.** (Troubles de la structure osseuse et lésions destructives au cours de la spondylarthrite ankylosante)
F. JACQUELINE. *Journal de radiologie, d'électrologie et Archives d'électricité médicale* [*J. Radiol. Électrol.*] **37**, 887–893, Nov.–Dec., 1956 [received Feb., 1957]. 5 figs., 18 refs.

The author describes how destructive lesions in the spine of patients with ankylosing spondylitis may present different appearances depending on whether the lesion is very active or stabilized. Two types of ankylosing spondylitis have to be distinguished. In the first there is a slow progress over many years; in this type osteoporosis is rare but there is marked bridging of the vertebrae. In the second type the progress is much more rapid and bridging of the vertebrae appears much more slowly, but there is marked generalized osteoporosis and ankylosis of the intervertebral articulations. The two types may occur in the same patient at different times.

Destructive lesions in the second, active, type are confined to the angles of the anterior vertebral margins. Destruction in the vertebral bodies may also sometimes be seen in stabilized cases following trauma, but in such cases is usually confined to areas where there is marked bridging of the vertebrae, whereas in the active type it may be diffuse. Three cases of ankylosis of the hip-joint with marked destructive changes in the femoral head are described. The term " destruction " in relation

to ankylosing spondylitis is really a radiological one, the so-called destruction being produced by intense osteoporosis and condensation. These appearances later disappear, to be replaced by bony ankylosis. In a few rare cases true anatomical destruction of the spine occurs, when it is similar to that found in the hip-joints.

John H. L. Conway-Hughes

RADIOTHERAPY

245. **The Radiotherapy of Cerebral Tumours.** (Die Strahlenbehandlung der Hirntumoren)
W. HELLRIEGEL. *Strahlentherapie* [*Strahlentherapie*] **102**, 21–30, Jan., 1957. 40 refs.

In this review from the University of Frankfurt am Main the radiosensitivity of cerebral tumours is first discussed and the advantages of focal therapy and particularly of pendulum oscillation therapy are stressed. For pituitary tumours convergent-beam therapy is preferred. The author's practice is to give a total tumour dose of 6,000 r at a dose rate of 200 r daily. In the event of a recurrence the dose of 6,000 r, or at least one of 4,000 r, may be repeated [but no further technical data are given]. The author's experience is based on 243 cases of cerebral tumour treated between 1945 and 1955. The series included 79 cases of pituitary adenoma (40 basophil, 13 eosinophil, and 26 chromophobe), 71 of glioblastoma, 21 of astrocytoma, and 15 of medulloblastoma. The results are discussed in some detail. Improved results were obtained when the tumour dose was raised in the later cases to 6,000 r or more. With the techniques described, some clinical improvement was obtained in about two-thirds of all the cases treated.

E. Stanley Lee

246. **Radiation Therapy of Neuroblastoma**
W. B. SEAMAN and M. D. EAGLETON. *Radiology* [*Radiology*] **68**, 1–8, Jan., 1957. 5 figs., 27 refs.

Writing from Washington University School of Medicine, St. Louis, Missouri, the authors review the most important literature on neuroblastoma in children and discuss the treatment and prognosis, pointing out that the latter has shown " remarkable improvements " in recent years. They then report that of 19 young patients with histologically confirmed neuroblastoma seen during the period 1949–55 and treated by irradiation, 7 have lived for periods varying from 10 to 76 months, 5 of them surviving for 45 to 76 months, a 3-year survival rate of 26%. In this group of 5, however, one patient now has metastases in the bones and another in the liver, in both cases confirmed microscopically. All the patients who died did so quite soon after treatment, usually without even a transient remission. In discussing the factors affecting the prognosis the authors point out that in the series under review all the 7 survivors were aged 17 months or less at the time of treatment. The literature reviewed confirms the opinion that the younger the patient, the better is the outlook. Gross in a large series found that in patients under 2 years of age the survival rate was 45% whereas in those aged over 2 years it was only 11%.

The complications of irradiation administered to young children are considered. In the present series a baby aged 2 months received a tumour dose of 3,120 r over 23 days by means of two fields each 10 × 10 cm. on the abdomen; this caused retardation of growth of the vertebral bodies, with fibrosis and atrophy of the erector spinae muscles resulting in spinal lordosis. In the authors' view the principle of therapy consists in an aggressive attack on all lesions, regardless of the extent of dissemination, tumour doses of 1,300 to 3,000 r being delivered over periods of 23 to 55 days. Leucopenia or debilitation may necessitate interruption of treatment. The question of irradiation promoting differentiation in this type of tumour is discussed. *Norman Mackay*

247. **Radiation Reactions in the Heart**
A. G. W. WHITFIELD and P. B. KUNKLER. *British Heart Journal* [*Brit. Heart J.*] **19**, 53–58, Jan., 1957. 3 figs., 6 refs.

From Queen Elizabeth Hospital, University of Birmingham, 4 cases are described in which irradiation of the thorax was followed by cardiac abnormality of uniform pattern, including constant T-wave inversion. The changes appeared at a time corresponding with the post-irradiation erythematous skin reactions. In 3 cases the changes disappeared within weeks; in the fourth case sudden death occurred, and no obvious cause was found at post-mortem examination. Two patients had *x*-ray bath treatment (2,900 r in 5 weeks and 2,700 r in 6 weeks respectively) and the electrocardiographic (ECG) changes corresponded with the homogenous dose distributed throughout the heart. In 2 cases irradiated after mastectomy with direct parasternal fields (4,000 r in 3 weeks) the highest cardiac dose fell on the anterior wall of the right ventricle, with corresponding ECG changes. These findings suggest that frequent ECG examinations would be desirable whenever radiation treatment involves high myocardial dose levels, and might provide a warning sign that the limits of cardiac tolerance have been approached. *J. Walter*

248. **Treatment of Hemangiomas with the Strontium-90 Beta-ray Applicator**
D. M. SKLAROFF. *Radiology* [*Radiology*] **68**, 87–89, Jan., 1957. 3 figs., 3 refs.

From the Albert Einstein Medical Center, Philadelphia, the author reports [with enthusiasm] the satisfactory results obtained in the treatment of superficial haemangioma in 10 infants by the use of an applicator containing radioactive strontium (^{90}Sr). The applicator consists of 25 millicuries of ^{90}Sr which is enclosed in a disk with an active area 7·8 mm. in diameter and covered by 2 mil (0·05 mm.) of stainless steel and 10 mil (0·25 mm.) of aluminium and is hermetically sealed. The shaft, 6¾ inches (16 cm.) long, is furnished with a movable, circular " plexiglass " protective shield ¼ inch (0·6 cm.) thick and 4 inches (10 cm.) in diameter. The output of the applicator is 34·6 r.e.p. per second and the 50% dose is at a depth of 1 mm. Doses of the order of 500 r.e.p. are administered by direct application of the source to a portion of the lesion. The excellent cosmetic

results obtained in 2 of the author's cases are described and illustrated.

[In infants the great majority of haemangiomata disappear spontaneously and it is the abstracter's view that, except for lesions interfering with function (for example, those on the eyelid), no treatment should be given. The very small diameter (7·8 mm.) of the active source in the apparatus described in this paper is a serious disadvantage.] *Norman Mackay*

249. **Interstitial Injection of Radioactive Colloidal Gold in Cancer: a Pilot Study**

J. S. KENNEDY, J. D. THOMSON, and F. C. WALKER. *Scottish Medical Journal* [*Scot. med. J.*] **2**, 105–110, March, 1957. 3 figs., 10 refs.

The authors of this paper from the University and Royal Infirmary, Glasgow, describe their attempts to treat lymph-node metastases from carcinoma by injection of suitable doses of colloidal gold. In some 25 cases, including cases of carcinoma of the breast, rectum, cervix, and bronchus, injections were given of tracer doses (0·5 to 1 mc.) of radioactive colloidal gold having a particle size of 20 millimicrons. Usually operation was performed a few days afterwards. Lymph-node tissue was examined histologically and by autoradiography. It was found that nodes which were completely replaced by carcinoma did not contain any gold. In some healthy nodes and in some of those only partially replaced by carcinoma there were variable amounts of gold, while in others no gold was found. In 8 cases of rectal carcinoma, in which the gold was injected through a proctoscope submucosally, there was no uptake of gold by any of the lymph nodes, a finding which the authors were unable to explain.

It is concluded that the results in cases of carcinoma of the bronchus and of the cervix were sufficiently encouraging to justify a further trial of this method of treatment. *E. Stanley Lee*

250. **Roentgen Therapy in Cushing's Syndrome without Adrenocortical Tumor**

F. C. DOHAN, A. RAVENTOS, N. BOUCOT, and E. ROSE. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **17**, 8–32, Jan., 1957. 7 figs., 19 refs.

The results of irradiation in 12 cases of Cushing's syndrome without adrenocortical tumour, seen at the Hospital of the University of Pennsylvania, Philadelphia, are presented. Only one of the patients had received surgical treatment previously, the left adrenal gland having been removed 9 weeks before irradiation, without improvement. In 5 of the 12 cases the results of irradiation were excellent, in 2 they were fair, and in 5 poor. In cases successfully treated some improvement was observed after 3 months, but marked improvement was noted only after 6 months.

In the 5 patients giving an excellent response the dose in "tissue roentgens" delivered to the centre of the pituitary fossa varied from 3,800 in 31 days to 5,250 in 52 days. A multiple-field technique was used [but no details of the size or arrangement of the fields are given]. One of the patients treated successfully later showed signs of hypophyseal insufficiency in the form of weakness and gross loss of weight, but recovered after a further 4 to 5 months. Other complications, including brain necrosis, are discussed.

From an analysis of these 12 cases and a number in the literature in which the data were adequate, it is suggested that an average daily input of about 100 r is more important than the final total dose in this treatment. Details of the authors' cases are given in an appendix, and photographs of the patients before and after successful treatment are reproduced. *J. M. Gibson*

251. **Carcinoma of the Cervix Uteri: Ten-year Study with Comparison of Results of Irradiation and Radical Surgery**

R. S. CLAYTON. *Radiology* [*Radiology*] **68**, 74–79, Jan., 1957. 1 ref.

The results of treatment in cases of invasive carcinoma of the uterine cervix seen at Parkland Memorial Hospital, Dallas, Texas, during the period 1944 to 1953 are analysed. Irradiation was carried out in 200 cases and surgery in 37 (including 6 cases in which both irradiation and surgical treatment were given). The clinical stage of the disease in 191 patients who received initial irradiation at Parkland Memorial Hospital was: Stage I, 24 patients; Stage II, 29 patients; Stage III, 75; and Stage IV, 63. Various combinations of external and transvaginal irradiation and intracavitary and interstitial radium were employed. (No details of the irradiation delivered are given.) Of the first 110 patients given irradiation the numbers alive at the end of 5 years were: Stage I, 13 out of 16; Stage II, 6 out of 15; Stage III, 8 out of 42; and Stage IV, 2 out of 37. There were no deaths attributable to irradiation. In 163 (81·5%) of the cases there was no appreciable morbidity; in 29 (14·5%) morbidity (proctitis and rectal stenosis) was moderate, but no prolonged treatment or surgery was required; while in 8 morbidity was severe—surgical removal of a radium needle (1), colostomy for rectal stricture (1), fistulae (4), prolonged skin ulceration (1), and intestinal obstruction from uterine adhesions (1). The average duration of stay in hospital in the irradiated group was 22·2 days.

Of the 37 patients operated on, 2 underwent pelvic exenteration; one of these died in the postoperative period, while the other died 4 years later, apparently from hepatic metastases. Radical hysterectomy with pelvic lymphadenectomy was performed in 35 cases, the operation being the initial treatment in 25. In 4 of the remaining cases in this group operation was performed for persistent or recurrent cancer after irradiation. No evidence of cancer was found in 13 (37%) of the specimens removed at hysterectomy; of these 13 patients, 5 had received irradiation. Altogether there were 5 postoperative deaths in the surgical group, while in 8 cases there was recurrence within 2 years of the last operation. The average stay in hospital in the surgical group was 47·5 days.

[The findings reported in this paper give further support to the view that irradiation is the treatment of choice in carcinoma of the cervix.] *Norman Mackay*

History of Medicine

252. **The Development of the Medical University at Montpellier to the End of the Fourteenth Century**
V. L. BULLOUGH. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **30**, 508–523, Nov.–Dec., 1956 [received March, 1957]. Bibliography

The term *universitas* originally signified a corporation or guild in general, but the meaning was narrowed to denote a learned corporation, and eventually was equated with *studium generale*—the university in the modern sense. In the 13th century Montpellier was one of three medical schools meriting the title of *studium generale*. Its origin is somewhat obscure, although medical study there was well established by 1137. This may have been because of its fortunate geographical position and its commercial importance. It was situated where it could be influenced by the Moslem schools of Spain, the Jewish schools of southern France, and the Christian school at Salerno. With changes in the ruling family there was no effective regulation of the school, and the ecclesiastical authorities assumed responsibility for its control, Montpellier being an important centre of Papal influence at that time. Regulations published in 1220 exemplify the formal organization of the school and the subjection of its authority to the Bishop. Conflicting interpretations as the school developed caused new statutes to be issued 20 years later.

The degree, although that of bachelor, was a graduate degree. It was awarded after 3½ years' study in Montpellier or in *alio loco famoso*, with 6 months' practice outside the town (for a Master of Arts the period was reduced by a year). After a public examination the successful candidate undertook to lecture at Montpellier for a further 2 years before leaving. Advanced degrees could be taken (Licentiate or Master), although the bachelor's degree alone was sufficient entitlement to practise. The Master's degree was equivalent to the Doctorate (which at that time was awarded only by Bologna). The period of study was 5 years for an M.A., or 6 years for non-graduates, with 8 months' actual medical practice. The candidate had to study and explain three set books out of a lengthy list, to give three lectures on the theory and practice of medicine, on which he was interrogated by the masters, and then to submit to a further oral examination on causes and their solution.

In 1289 Montpellier received recognition as a *studium generale* in a Papal decree which went on to require all masters to give public oath to the Bishop before receiving permission to teach. In 1340 the university statutes were re-codified, and they give interesting information on the division of the masters into those who were required to teach and those who were not, and on the manner in which students were assigned to them, and on how the teachers selected the books on which they proposed to lecture. It is notable, too, that all students were now required to attend mass daily (which has caused controversy over whether or not non-Christian influences could have been effective in the earlier period). Students were required to record their dates of arrival and departure, and were strictly limited to the study of medical subjects; it was, in fact, forbidden to take an arts degree after taking a medical degree. The dissection of a human body was required by the university every 2 years, although this does not seem to have been effectively carried out until nearly the end of the century.

Surgery at Montpellier followed an independent course, having been specifically excluded from the application of the statutes of the medical university in 1239. In 1399 Charles VI forbade the practice of surgery to anyone—other than a member of the university faculty—who had not submitted to examination by a group of masters. There is little information on the development of surgical teaching, which was probably extramural. In the 15th century masters of medicine were forbidden to practise surgery.

" Montpellier by the end of the 14th century had more or less perfected its organization . . . Medicine was now considered a graduate study with some arts training a prerequisite . . . The importance of Montpellier lies in the fact that there medicine gave rise to the concept of a modern university and medicine was put alongside other schools in the university curriculum. An understanding of the development of Montpellier also gives some indication of how and why some of our present academic traditions developed." *Geoffrey R. Pendrill*

253. **Van Helmont's Ideas on Gastric Digestion and the Gastric Acid**
W. PAGEL. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **30**, 524–536, Nov.–Dec., 1956 [received March, 1957]. Bibliography.

Van Helmont's discovery of the principles of gastric digestion and his identification of the active agent as hydrochloric acid have not hitherto received proper recognition. His treatise *Calor efficienter non digerit* (1648) rejected the Galenic concept of heat as the digestive principle and put forward arguments in support of a contention that it was some form of strong acid. This acid, however, was thought to be specific to the individual, as shown by variations in dietary tolerances. The Galenic idea of " concoction " (πέψις) was a process whereby the heat engendered by the organs surrounding the stomach reduced food to a state in which it was assimilable by the body, acid black bile from the spleen assisting in the process. To Van Helmont the relative importance of these two factors was reversed, since heat was a non-specific principle, whereas the nature of the gastric principle—acid—was clearly specific.

Contemporary views on Galen's theories, as represented in Fernel's *Universa medicina*, differ somewhat from the original. Here the liquefaction of food is caused by heat, but its " concoction " is attributed to

some occult (but undefined) quality of the gastric substance, and is specific. While this obviously anticipates Van Helmont's ideas, it does not go so far as to identify the active principle as an acid. Van Helmont perhaps owes something to Paracelsus, who stated (in a passage with which Van Helmont was familiar) that acid present in mineral waters was an adjuvant to gastric digestion, and useful in the cure of the stone; he credited ostriches with *acetosa esurina* (" appetizing acids "), which enabled them to digest iron. Nevertheless, Van Helmont goes farther in attributing an *acidum esurinum* to all animals and to man, and in regarding this as a specific agent peculiar to the stomach. He rejects Fernel's idea of " black bile " as the source of this acid, but states that the properties Fernel attributed to it are exactly those of aqua fortis—hydrochloric acid or " spirit of salt ". Salt compounds are generally of an acid nature and moreover have the property of stimulating appetite and promoting digestion. Van Helmont was acquainted with hydrochloric acid, which he had been led to prepare as a cure for calculus after having observed the stone-dissolving properties of the gastric juice of pigeons. From this we may infer that he identified the gastric acid as hydrochloric acid.

In conclusion it is interesting to note that underlying Van Helmont's theory are fragments of alchemistical philosophy. He describes the digestive process in terms of a transmutation of one substance into another by a spiritual agent (a ferment) assisted by heat. This is reminiscent of descriptions of the Philosophers' Stone. Despite this, it should be stated that Van Helmont's chief claim to fame is that whereas the alchemists explained inorganic processes in terms of the processes of organic life, he was a pioneer in the application of organic chemical patterns to biological processes.

Geoffrey R. Pendrill

254. **A Contribution to the History of Infants' Feeding Bottles.** (Beitrag zur Kenntnis der Trinkgefässe in der Kinderpflege)

A. HOTTINGER. *Annales paediatrici* [*Ann. paediat. (Basel)*] **187**, 437–443, Dec., 1956. 5 figs., 11 refs.

The artificial feeding of infants appears to have been employed from very early times. The earliest known drinking vessel dates from the Neolithic Age, and later vessels date from the Bronze Age and have appeared in Etruscan finds. In Roman times they were sometimes made of glass, and specimens have been found in the graves of children in many of the countries at one time under Roman occupation.

Writing from the Kinderspital, Basle, the author describes a glass bottle in his possession which dates from the early 19th century. Its shape is elongated, reminiscent of the modern boat-shaped bottle. When in use, a piece of leather, linen, parchment, or a prepared cow's teat was tied to the open end. In the back of the bottle was another aperture, the opening and closing of which by the thumb controlled the flow of milk. The author then describes and illustrates an earthenware vessel made in the shape of a fish, again with a hole in the back, which was found in the tomb of a Babylonian child, and also an upright glass bottle with a hole in the side and furnished with a tin nipple which was used in the 18th century. Apart from these infants' feeding bottles, a number of glass vessels used for emptying the breasts after delivery are described. These date from the 16th century and are globular glass bottles with an opening shaped like a shallow funnel which was pressed to the nipple, and in addition a long narrow spout, through which the mother herself applied suction to the breast. Thjs treatment was apparently thought necessary for stimulating the onset of the flow of milk.

Marianna Clark

255. **The Health of James the Sixth of Scotland and First of England**

A. L. GOODALL. *Medical History* [*Med. Hist.*] **1**, 17–27, Jan., 1957. 2 figs., 35 refs.

King James is remembered in the history of medicine for his grant of charters to the Royal Faculty of Physicians and Surgeons of Glasgow and the Society of Apothecaries, and for his book *Counterblaste to Tobacco*. His policies as a monarch were so complex that the influence upon them of his state of health makes an interesting study.

His birth in Edinburgh Castle on June 19, 1566, was attended by doubts as to his parentage, but there is no evidence to support the gossip that Rizzio, the favourite of his mother, Mary Queen of Scots, was his father. It has also been rumoured that James was a changeling; this might explain some discrepancies of character, yet some of his physical features, such as the long jaw, were those of the Stuart family. At the age of 13 months, James was crowned king, and in consequence his youth was darkened by the struggles of different factions to control his person. About the age of 20 he was described as well educated in languages, science, and affairs of state; his worst failings were extravagance, laziness, and great love for favourites, this last, based on physical attraction, being in evidence throughout his life.

The best account of James's health in early years was provided by Sir Theodore Mayerne in 1623 in the form of a past history. He wrote that James was suckled by a drunken wet nurse for a year, that he could not walk until he was 6 (a possible indication of rickets), by which time he had already had smallpox and measles, that at 5 years he had a suppression of urine for 24 hours, and that he suffered frequently from colic and diarrhoea. It was said in 1589 that James was not interested in women, but state policy demanded his marriage with Anne of Denmark. Of their family, Henry, Elizabeth, Charles, and Robert were healthy children; Anne had one miscarriage, while 3 other children died in infancy.

On March 24, 1603, James succeeded to the throne of England. On the journey south he fell from his horse and broke a collar-bone. Contemporary descriptions of the new king, as might be expected, are over-flattering; in fact he was plump, with a ruddy complexion, his hair was light brown tinged with white, while his beard was thin. His example to his new court was unfortunate; his manners became coarse and personal cleanliness a rarity. James, while not a chronic alcoholic, was often drunk. Following Prince Henry's death in 1612, the king suffered severe grief and melancholy, accompanied

by digestive disorders, probably occasioned by his passion for fruit. From the age of 45 onwards he was the victim of increasingly frequent attacks of nephritis, arthritis, and gout. He itched insufferably, and was subject to frequent colds and bronchitis. Wasting and pain in the legs probably indicated atherosclerosis; he passed three urinary stones. Other complaints included haemorrhoids, insomnia, enlarged right axillary lymph nodes, and a right olecranon bursitis. From the age of 50, James lapsed into repulsive senility. He died in 1624, after suffering from arthritis and an ague, his last hours being marked by a stroke, a swollen tongue, and diarrhoea. The charge that he was poisoned by Buckingham rests on very inconclusive evidence. The post-mortem revealed one completely shrunken kidney.

Arthritis, pyelonephritis, and atherosclerosis must all have had considerable effect on James's temperament and mental abilities. The insecurity of his youth probably had repercussions on his psychological state, while the indulgence in favourites may well have sprung from a lack of affection in childhood. *F. M. Sutherland*

256. **The Historical Aspects of Venous Thrombosis**
S. T. ANNING. *Medical History* [*Med. Hist.*] **1**, 28–37, Jan., 1957. Bibliography.

Phlegmasia dolens in the lower limb is the particular aspect of venous thrombosis the historical aspects of which are dealt with in this paper. Virchow established a triad of factors concerned with venous thrombosis—lesions of the vascular intima, changes in the bloodstream velocity, and alteration in the constitution of the blood. The historical development of this concept is traced, and reasons are given for the rarity of clinical descriptions of post-partum phlegmasia dolens before the 18th century.

About 2,650 B.C., Huang Ti wrote about the blood coagulating "within the pulse", but this may have referred to arterial thrombosis. Descriptions of puerperal fever in the Hippocratic writings contain no mention of swollen limbs. The term, "leucophlegmatia", used by Hippocrates and other ancient authors, covered a variety of oedematous conditions and may have been used to describe phlegmasia dolens. Aristotle does not mention the disease, but observes that the coagulation of blood depends on the presence of fibrous material. Galen introduced the term "thrombosis", but little advance in the subject was made by Graeco-Roman authors or during the mediaeval period. However, in one of the *Consilia* of Ugo Benzi, written about 1400, there is a description of venous thrombosis occurring during a long illness. Medical theory at this time was dominated by Galen's doctrine of humoral pathology, and there are frequent references to the collection of corrupt humours in the legs. Thus Jean Fernel in the 16th century attributes oedematous ulcers of the leg to such humours. Menstrual blood was believed to be an evil humour, and Ambroise Paré considered swollen legs in pregnant women to be due to suppressed menses. Following the same line of thought, such authors as Roderiguez a Castro of Hamburg and François Mauriceau of Paris held that the lochia were bad humours the retention of which caused swelling in the legs. The humoral theory was also the basis for the idea expressed by Puzos in 1759 that the excess milk formed in women and not consumed by the foetus in utero or the infant at the breast collected and caused lesions in the lower limbs. This conception explains the term "milk leg", still in current use.

During the 17th century, Richard Wiseman furnished descriptions of both phlegmasia dolens and venous thrombosis. Researches were made into the pathology of coagulation by Leeuwenhoek, who described and measured the red blood corpuscles, and by Malpighi, who found the fibrous part of the clot. In 1628 a fundamental blow was struck at the humoral theory by Harvey's demonstration of the circulation of the blood, and the new iatro-mechanical school put forward its own explanation of post-partum phlegmasia. Thus in 1784 Charles White attributed it to an accumulation of lymph in the limb, due to rupture of the lymphatics from pressure of the head of the foetus during labour. During the late 18th century John Hunter, William Hewson, and Matthew Baillie all did valuable work on the coagulation of blood. During this period pathophysiological ideas replaced the purely mechanical approach to medicine. In 1800 Hull reviewed the literature of what he named "phlegmatia dolens", and the term "phlegmatia alba dolens puerperarium" was first used by White in 1801. In 1815 Hodgson noted that injury to a vein might cause extensive thrombosis.

Davis of Queen Charlotte's Hospital, London, in 1822 was the first to demonstrate the veins as the cause of the trouble in phlegmasia dolens; in 1829 Lee showed that the disease began as phlebitis in the uterine veins and spread to the iliac and femoral veins. In 1853 Lee also indicated the factor of complicated labour with intrauterine manipulation. Rokitansky in 1852 differentiated venous thrombosis due to injury or inflammation from that due to changes in the blood itself. A year later Mackenzie published a full clinical account of post-partum thrombosis, and recent research has confirmed his conclusions that the disease is more common after difficult labour combined with instrumental delivery, puerperal sepsis, or haemorrhage, while a further factor is the inevitable slowing of the venous blood flow in the legs during rest in bed and parturition.

The lack of references to the disease before the 18th century may be explained by the high maternal mortality in abnormal cases, while the midwives invariably employed were unlikely to describe their experiences. In addition, the common use of forceps after the mid-18th century, while reducing mortality, made phlegmasia dolens more common. *F. M. Sutherland*

257. **Theodore Billroth as a Historical Figure. An Unpublished Letter to Francesco Rizzoli.** (La figura di Teodoro Billroth e una sua lettera inedita a Francesco Rizzoli)
E. DALL'OSSO. *Policlinico, sezione pratica* [*Policlinico, Sez. prat.*] **64**, 235–240, Feb. 18, 1957. 2 figs., 9 refs.

258. **The Plague in Cambridge**
R. WILLIAMSON. *Medical History* [*Med. Hist.*] **1**, 51–64, Jan., 1957. 37 refs.